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DIFFERENTIAL DIAGNOSIS OF LEAKING RETROPERITONEAL ANEURYSM.

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NOT many years ago, the diagnosis of leaking retroperitoneal aneurysm was considered to be of interest because the unfortunate sufferer would then know that *he had a "lucid interval to put his affairs in order"* (Copping, 1953).

Although a leaking aneurysm in this site still has a high mortality, the condition can be treated with some prospect of success if the diagnosis is made before the patient becomes moribund. Morris (1958) in Australia reported 15 cases with survival in nine. The reported series (Baird, 1953; Betts, 1953; Copping, 1953; Estes, 1950; Reed, 1955; Blakemore, 1947) as well as the present show that death rarely occurs so rapidly from a leaking retroperitoneal aneurysm that surgical treatment is impossible. The mortality of this condition untreated is 100%. The condition is also of interest because the incidence is likely to increase in any aging population, as the incidence of atherosclerotic aneurysms increases (Maniglia and Gregory, 1952).

Clinical Features.

We present here an analysis of 13 cases of ruptured abdominal aortic aneurysms producing retroperitoneal hæmatomata, one case of ruptured aneurysm of the splenic artery, and one case of aortic aneurysm rupturing into the œsophagus. Cases of dissecting aneurysm of the aorta rupturing retroperitoneally are excluded, although some of the data from another series of dissecting aneurysms have been used for comparative purposes where indicated. The patients were admitted to the Royal Prince Alfred Hospital between 1950 and 1958. In the cases reported, a fairly characteristic clinical pattern emerged. Of the 15 patients, 12 were male and three were female (a ratio of 4:1). The average age in the series was 70 years (minimum 56, maximum 80). Seven patients gave a past history of abdominal pain or mass, six of hypertension. In six cases the presenting symptoms had been present for more than 24 hours. The symptoms are set out in Table I.

A variety of incorrect diagnoses had been made in these cases. They included myocardial infarction, perforated peptic ulcer, pancreatitis and intestinal obstruction.

Prior to their admission to hospital, symptoms suggestive of an abdominal aneurysm had been present in half the patients, five of whom had been known to have a pulsating abdominal mass present. Pain without shock had occurred periodically over a number of weeks or

months prior to admission in six other cases. In a further four cases, the immediate symptoms had been present for only 48 hours or less before admission to hospital.

All patients presented with pain. This usually had a sudden onset, was severe and persistent, and was often punctuated by periodic exacerbations. It was associated with shock and vomiting. The first sign in many cases was the sudden onset of collapse with severe pain. The patient was cold and restless and sweated profusely. Indeed, shock occurred sooner or later in all subjects coming to autopsy. It did not always occur simultaneously with the onset of the severe pain. In some cases the patient was admitted to hospital complaining of pain and vomiting without shock, only to develop it after a few hours. Four such patients were in pain before shock had ensued; on three of these operation was not performed immediately, shock then developed, and death followed.

TABLE I.

Symptoms and Signs.	Number of Cases.
Symptoms:	
Pain (severe, sudden onset, 11; back, 8; umbilicus or iliac fossa, 7; epigastrium or hypochondrium, 6; inguinal region or testis, 4; chest, 2)	14
Shock	14
Vomiting	8
Hæmatemesis	3
Melæna	2
Cold, painful legs	1
Shoulder-tip pain (hæmoperitoneum)	1
Oliguria	1
Signs:	
Abdominal tenderness	9
Abdominal distension	7
Abdominal guarding	5
Pulsating abdominal mass	6
Non-pulsating mass	3
Subnormal temperature (less than 90° F.)	6
Absent femoral pulses	3
Bruised flanks or Cullen's sign	2
Dilated abdominal veins	2

The pain most commonly occurred in the back, or in the lumbar or sacral region. The next most common site was the umbilical zone or the iliac fossa, and then the epigastrium. Pain in the inguinal region or in the testis was less common. In most cases the pain commenced in one site and later spread to others.

An expansile pulsating abdominal mass was present in only six out of the 15 subjects, but another three had a non-pulsating tender mass. Localized abdominal tenderness and abdominal distension were common, but in only five cases was there any muscle guarding. The unusual occurrence of severe abdominal pain without abdominal rigidity is worthy of notice.

Four patients had bruising of the loin, or Cullen's sign, or dilated abdominal veins.

Signs of arterial occlusion were more common in dissecting than in leaking aneurysms. Two of the patients in the latter group complained of cold, painful legs, and their femoral pulses were absent. In eight cases of dissecting aneurysms which ruptured retroperitoneally, symptoms due to vascular occlusion occurred in five; these included hemiplegia, mesenteric infarction and absence of femoral pulses, with gross peripheral ischæmia.

One patient presented with the history of vomiting bright red blood on several occasions during the previous nine days. He was not suffering from shock on his admission to hospital, but shock soon developed after a massive hæmorrhage. Emergency gastrectomy was performed before it was discovered that the hæmatemesis was due to the rupture of an aneurysm into the œsophagus.

In another case melæna resulted from rupture of an aneurysm into the terminal portion of the ileum. Shoulder and shoulder-tip pain were noted, as well as increased frequency of micturition on occasions.

A white cell count was performed in only two cases. In one the figure was normal, and in the other it was elevated to 25,000 per cubic millimetre. The hæmoglobin concentration was within normal limits.

Once a patient became shocked, the outcome usually was either death within a few hours, or recovery, succeeded by another episode of pain and severe shock within 48 hours, which this time was fatal. Two patients survived for longer periods after the initial episode, the intervals being one and four months respectively. However, in both cases the initial symptom had been pain unaccompanied by collapse. With the exclusion of these two patients, and of the two on whom operation was successful, the average length of life after admission to hospital was 16 hours.

Reports of Cases.

CASE I.—A man, aged 71 years, developed pain in the right testicle three days before his admission to hospital. This spread into the right side of the abdomen, the right leg, and the back; it was severe and constant, with periodic exacerbations. On admission he was cold, clammy and restless. Hypotension (blood pressure 90/70 mm. of mercury), a pulse rate of 90 per minute and a subnormal temperature (95° F.) were recorded. His abdomen was distended, bowel sounds were present, and there was a tender, non-pulsatile mass in the right iliac fossa. He vomited a little blood and bile-stained material. The thigh and lower abdominal wall gradually became deeply bruised, and distended superficial abdominal veins were present. Laparotomy was performed, and the aneurysm was deemed inoperable. He died 18 hours after admission. At the post-mortem examination a large retroperitoneal hæmorrhage was present, originating from a ruptured atherosclerotic aneurysm of the right common iliac artery.

CASE II.—A man, aged 64 years, complained of a continuous aching pain in his back of eight hours' duration. On two occasions this had become severe, and had spread from the right loin into the right thigh. Neither shock nor vomiting was present. His pulse rate was 80 per minute, his temperature was 98° F., and his blood pressure was 110/70 mm. of mercury. His femoral pulses were palpable, but his feet were cold and the ankle pulses were absent. A pulsating epigastric mass was present, with some tenderness and guarding on the right side of the abdomen.

Operation was commenced within four hours of his admission to hospital and retroperitoneal blood clot, originating from a leaking aortic aneurysm, was found spreading into the small-bowel mesentery. The aneurysm extended from below the renal arteries into the right common iliac artery. The whole affected area was resected, and an Edwards-Tapp bifurcated crimped nylon graft was inserted. He was discharged from hospital three weeks later, and was symptom-free when examined three months after operation. At this stage all the peripheral pulses were palpable and normal.

CASE III.—A man, aged 75 years, was known to have had an abdominal aneurysm for three years. There had been attacks of pain associated with this over these years. Ten hours prior to his admission to hospital he had suffered sudden severe epigastric pain. On his admission, he was very pale and obviously distressed. His pulse rate was 120 per minute, and his temperature was subnormal (94° F.). Shock was so profound that the blood pressure could not be recorded. His abdomen was distended, and a large, pulsating, tender epigastric mass was present. The femoral pulses were not palpable. Operation was performed immediately, and a ruptured aortic aneurysm was found. It was situated below the renal vessels, so that excision and grafting were performed. After operation the blood pressure was not able to be maintained, and the patient died 14 hours after his admission to hospital.

Discussion.

A leaking abdominal aortic aneurysm may present in a variety of ways. However, in spite of their variety—indeed, because of it—these cases have much in common. The following are some of the misdiagnoses reported in the literature: psoas abscess (Eckert and Baker, 1931); hæmatemesis from chronic peptic ulcer (Roll and Candell, 1956); intestinal obstruction (Van Meurs, 1948; Mayo, 1951; Cuny, 1937); strangulated inguinal hernia (Betts and Rowlands, 1953); acute cholecystitis or biliary colic (Osler, 1905); ruptured viscus (Copping, 1953; Jellinek,

1956); organic disease of the gastro-intestinal tract (Baer and Loewenberg, 1948); coronary occlusion (Jellinek, 1956).

Although the foregoing list suggests that the diagnosis of leaking retroperitoneal aneurysm may be somewhat difficult in the early stages, there are several features which should help to establish it once it has been considered. The features which can be ascribed definitely to an aortic aneurysm vary from a throbbing sensation in the abdomen to a mass, perhaps discovered by accident, or a readily appreciated pulsating abdominal swelling.

On being closely questioned the patient may have observed various symptoms suggestive of either central or peripheral vascular degeneration before the symptoms due to rupture supervened.

There may have been abdominal discomfort—a deep ache or boring sensation (Morris, 1958), or possibly quite severe pain. The presence of continuing pain does not necessarily mean that an aneurysm is about to rupture (Bahnson, 1956; Ellis and Kirklin, 1956; Barnes *et alii*, 1953). However, abdominal aneurysms are not infrequently symptomless until the moment of rupture (Blakemore, 1947; Crane, 1955), as in six out of the present 15 cases. Blakemore believed that atheromatous aneurysms in the aorta were painless, because they tended to enlarge forwards and consequently did not cause much pressure on the vertebral bodies. The condition is more common in men than in women, in the ratio of about five to one (Crane, 1955). The majority of the men so afflicted are aged over sixty years, although occasional cases have been reported in men in their fifties.

The major presenting symptom of rupture is nearly always acute severe pain. This may begin while the patient is at rest; but instances are reported in which the onset followed an injury (Shumacker, 1955) or while the patient was taking moderate exercise, such as digging. The onset is usually sudden, sometimes quite dramatically so, with a sensation that something has burst or torn internally (Farrar *et alii*, 1958; O'Malley, 1957), or it may be spread over a few minutes or even half an hour. The site of the pain may be misleading at first. It may start in the chest and then move quickly into the abdomen—a sequence which is particularly likely if the aortic wall first dissects in the thorax and later ruptures in the abdomen (Cope, 1957). The pain may begin more centrally, either in the umbilical or the epigastric regions. Frequently the pain starts in the back (Wheelock and Shaw, 1956), often in the lumbar region. When there is both abdominal and back pain the latter component is usually the more severe. At the outset pain in the buttock or over the sacrum is unusual; but later, as the hæmorrhage spreads, it becomes quite common. Pain in the testicle (Wheelock and Shaw, 1956) may also be a first symptom of rupture.

After the initial period of pain, which may last six or eight hours, the patient's condition often improves, for as long as 24 or even 48 hours. Then there is a sudden return of pain, which is just as severe as it was at first, but commonly is centred on another area. For instance, if the pain was originally most severe around the umbilicus, on return it may be most acutely felt in the lumbar region; or if the initial pain was in the back, the second attack may be much worse over the sacrum, in the buttocks or in the medial side of the thigh. Alternatively, the patient may after a few hours have a period in which the pain is easier, but after this short period of relative freedom it returns for a third time, when it may be more severe and in another site, although usually after the second episode it becomes fairly widespread, and in subsequent episodes the pain is more diffusely distributed.

Although the patient may complain of pain and discomfort in the region of the aneurysm before it has leaked, that which occurs at the time of the rupture is much more severe and of a different quality; its character is apparently difficult to describe because of its agonizing severity—such words as "excruciating", "terrible", or "horrible" are used by patients. On close questioning of the patient the pain is not usually described in a way suggestive of intestinal, biliary or renal colic, in that it does not occur in waves or spasms with moments of freedom in between severe bouts, but is constant for several hours while at its height. The patient rarely moves about vigorously in bed or walks about as though suffering some form of colic. It is uncommon for more than three episodes of pain to be experienced before the final fatal rupture. This usually occurs within a few days, although some cases have been reported in which the patient survived for some weeks. In the present series one patient survived for one month and another for four months, though their initial symptom was pain unassociated with a very severe degree of shock. It is reasonable to suppose that in these cases the leak was minimal and that subsequent thrombosis and fibrosis of the weakened area occurred.

A profound degree of shock is commonly associated with the pain. The elderly man who has been diagnosed as suffering from a perforated peptic ulcer, and who collapses in the X-ray department, should be suspect of harbouring a leaking retroperitoneal aneurysm. The systolic blood pressure is nearly always below 100 mm. of mercury, and not infrequently, particularly after the second attack of pain, below 70 mm. This hypotension may be comparatively minor in the first bout of pain, but in subsequent attacks is always of major degree. The most obvious feature in the appearance of the patient is an extreme death-like pallor, which is much more marked than that seen when the underlying condition is a perforated peptic ulcer or renal colic. During the intervals between the episodes of pain the blood pressure may rise to almost normal levels; but each successive bout of pain is accompanied by progressively graver falls in blood pressure. This may well be due to disruption of the splanchnic innervation rather than to actual blood loss.

The diagnosis is made relatively simple if, in addition to the above-mentioned signs and symptoms, a pulsatile tumour can be felt in the abdomen. However, a mass may sometimes be felt in the loin or in the iliac fossa on one side, and this may or may not pulsate. It is often more readily felt under anæsthesia. If the mass pulsates it may be the aneurysm itself which can be felt; in this case it is usually situated in the mid-line, with its long axis down the mid-line of the abdomen. Occasionally an aneurysm occurs which is confined to the common iliac artery, and this may be felt in the iliac fossa (Crane, 1955; Betts and Rowlands, 1953). A mass in the flank or in the iliac fossa is frequently non-pulsatile, as it is composed of hæmatoma, into which the aortic pulse wave is introduced only during the actual period of leak from the aorta. The amplitude of pulsation in the hæmatoma may be considerably reduced by the pronounced fall in blood pressure and may be difficult to detect because of the surrounding blood clot and the presence of muscle guarding. If the patient or his doctor previously noticed an abdominal swelling the onset of the hæmorrhage may coincide with a sudden increase in its size or with the appearance of a second swelling.

During the first episode of pain the patient may vomit; but vomiting is usually not a marked feature, nor is it as persistent as in acute pancreatitis or small-bowel obstruction, unless the duodenum is obstructed by an accumulation of blood clot around it, as Javid *et alii* (1955) reported. Several cases are recorded in the literature (Roll and Candell, 1956; Ross and Pheils, 1957; Reed, 1955) in which the aneurysm has ruptured into the gastro-intestinal tract. The most common site of rupture into the bowel is the third part of the duodenum, where it lies directly related to the front of the aorta. There are, however, cases in which the aneurysm perforated into the ileum (Baird, 1953) or stomach (Kampmeir, 1936). In the present series, in one case it discharged into the ileum and in another into the œsophagus. When such ruptures occur the patient frequently vomits blood; but even on these occasions he may live for several hours before the hæmorrhage becomes fatal. However, a hæmatemesis or melæna does not invariably imply a direct

communication between the leaking aneurysm and the gut. The dissection of the aortic wall even for a short distance, which precedes the rupture, may obstruct the mesenteric arteries and so produce considerable effusion of blood into the lumen of the bowel, which is subsequently revealed either as hæmatemesis or melæna.

After the onset of the first bout of pain, either the patient or his medical attendant may notice increasing abdominal distension due to paralytic ileus. This has been described, and to some extent investigated experimentally, by French authors (Lenormant and Cordier, 1934; Tixier and Clavel, 1932). The bowel sounds are somewhat variable in this condition. During the stage of shock they may be absent, and if there is paralytic ileus they remain absent. If the intestines are distended, the bowel sounds may be metallic (Christensen, 1958); or if their lumen is full of blood the sounds produced may be turbulent or "sloshy", as occurs when there is bleeding into the bowel from a peptic ulcer (Milton, 1958).

On examination of the patient, apart from the obvious and severe pallor and feeble pulse, the abdomen may be tender. This tenderness is either roughly localized and apparently related to the area of effusion or quite diffuse. Abdominal distension may be observed and a mass may be felt. In addition, bruising may be seen on the lower part of the abdominal wall, in one or other flank, or on the anterior surface of the thighs. This bruising apparently is caused by direct extension of the blood extravasated from the aneurysm, and is similar to that seen in other conditions in which this occurs — e.g., acute pancreatitis. Occasionally the blood accumulates in the inguinal regions to such an extent that a diagnosis of strangulated inguinal hernia has been made (Betts and Rowlands, 1953). The abdominal rigidity associated with perforated viscera is of much greater degree than that observed in the early stages of a leaking retroperitoneal aneurysm. However, the intense pain may give rise to the sensation of rigidity; but this relaxes during inspiration. Sooner or later, blood bursts through the peritoneum and then the features of peritoneal irritation may be marked (Beebe and Powers, 1958). However, by this time the end of the chapter has been reached.

In two cases in the present series distended veins were seen on the lower part of the abdomen after the most severe bout of pain, and it appears that these may be collateral channels which have become dilated as a result of the obstruction to the inferior vena cava. Direct involvement of the caval wall in the spreading clot occurs, with partial or complete compression.

An electrocardiographic examination is frequently made in these cases, and if any abnormality is detected, it is usually reported as being suggestive of cardiac ischæmia, and possibly of a posterior wall infarct. However, there do not appear to be any electrocardiographic findings which prove or disprove the diagnosis of leaking aneurysm.

In patients who have had their symptoms for a day or two, the white cell count may be raised to 25,000 per cubic millimetre or even more. This does not indicate that there is any secondary infection in the hæmatoma, but it is simply a non-specific response to a large collection of effused blood.

A plane X-ray film of the abdomen is useful in this condition, because it may give evidence which is negative but relevant by excluding radio-opaque renal or biliary calculi or the presence of gas under the diaphragm. It may reveal positive evidence of calcification which can be seen in the wall of the aneurysm (and this can often be seen best in a lateral film) when the bony outlines do not obscure the calcification. In the antero-posterior film, the loss of the psoas shadow may also be of value. In addition, there may be radiographic features of ileus with an accumulation of gas in both small and large bowel.

Summary.

We present here an analysis of 13 cases of ruptured abdominal aortic aneurysms producing retroperitoneal hæmatomata, one case of ruptured aneurysm of the splenic artery and one case of aortic aneurysm rupturing into the œsophagus. Cases of dissecting aneurysm of the aorta rupturing retroperitoneally are excluded from this series, although some of the data from another series of dissecting aneurysms have been used for comparative purposes when indicated.

The clinical picture of a leaking retroperitoneal aneurysm is characteristic, and has features which enable the diagnosis to be made even in the absence of a palpable mass. The first of these features is intense abdominal pain of excruciating severity, which comes in a series of attacks, the position of the pain tending to vary between the first and second attacks; the greatest pain may be in the back or over the sacrum, but the pain may occur anywhere in the abdomen, or in the thigh or in the testicle. Associated with the pain is a very severe degree of shock, which is far more marked than in most of the conditions with which leaking retroperitoneal aneurysm is likely to be confused. Other features are bruising in the flank or thigh, and the presence of tender, pulsatile or non-pulsatile masses in the inguinal region, the iliac fossa or the flank.

Other signs and symptoms are discussed. The X-ray evidence is of both positive and negative significance.

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TRACHEOSTOMY IN CHILDHOOD.

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TRACHEOSTOMY may be indicated for the relief of respiratory tract obstruction due to a wide variety of conditions. These conditions may be divided into two groups. The first group comprises conditions in which there is actual mechanical obstruction, for which tracheostomy provides a "by-pass". The second group comprises conditions in which obstruction occurs as the result of pooling of secretions in the respiratory tract. Various factors, such as unconsciousness, pain and paralysis, may contribute to this. In such circumstances tracheostomy provides a convenient means by which the secretions may be aspirated and the airway kept clear.

Subdivision of respiratory tract obstruction requiring tracheostomy into such groups has been made by Nelson and Bowers (1957), who termed the groups "mechanical ventilatory obstruction" and "secretional ventilatory obstruction".

There are a variety of conditions responsible for mechanical obstruction in the child. The mechanical obstruction in which tracheostomy may be indicated may be infective, such as acute laryngo-tracheo-bronchitis, *Hæmophilus influenzæ* type B epiglottitis or laryngeal diphtheria; or the obstruction may be due to some other cause, such as a foreign body, trauma (including endoscopy), congenital anomalies of the larynx and upper part of the respiratory tract, laryngeal tumours, laryngeal hæmorrhage, allergic œdema, bilateral recurrent laryngeal nerve lesions, "laryngeal spasm" of undetermined ætiology and extrinsic pressure, e.g. congenital goitre.

Examples of conditions in which secretional obstruction may occur are head injury, cerebral tumour, encephalitis, tetanus, poliomyelitis, polyneuritis and chest injuries.

A series of 28 consecutive tracheostomies were performed at the Royal Children's Hospital, Melbourne, between December, 1955, and April, 1957, inclusive. The age range of the children was from 4 weeks to 12 years. Primary infective conditions (laryngo-tracheo-bronchitis, *H. influenzæ* epiglottitis and diphtheria) formed a high proportion of the cases (12 of the 28). Five cases were due to obstruction following endoscopy or endotracheal anæsthesia; five cases were due to other obstructive conditions, and six cases were due to miscellaneous conditions with secretional obstruction.

Indications for Tracheostomy.

In the group with secretional obstruction, tracheostomy may be performed for existing or for potential obstruction. In the latter event, the indications are concerned with the nature and severity of the patient's primary condition and with its likely effect on respiratory tract function. Tracheostomy then assumes a prophylactic role. If obstruction is already present, its manifestations resemble, in many ways, those of the first group — mechanical obstruction.

With mechanical obstruction the decision to perform tracheostomy must be related to the degree of obstruction actually present. The severity of the obstruction may be assessed from its effects. Of these, the most important possible effect is the development of anoxæmia.

Stridor is often a striking feature of laryngeal or tracheal obstruction. While its pattern may be of help in localizing the obstruction, it is not always useful in assessing its severity. The intensity of the stridor varies both with the degree of obstruction and with the effectiveness of ventilation. Thus stridor may be faint when the obstruction is severe.

Retraction, also a striking feature of certain types of obstruction, varies again with the ventilatory effort. While marked sternal retraction means severe obstruction, mild retraction may occur with equally severe obstruction because of poor ventilatory efforts. In addition, the typical sternal and suprasternal soft tissue retraction of laryngeal obstruction may be modified by coexisting obstruction in the smaller bronchi, as in some cases of laryngo-tracheo-bronchitis. Consequent emphysema may prevent the development of the usual sternal retraction.

If ventilation is sufficiently impaired, anoxæmia results. The principal effects of anoxæmia are on the circulatory system, causing initially tachycardia and later circulatory collapse, and on the brain causing first restlessness and later depression of consciousness. Finally, death occurs from respiratory failure.

Quite severe lack of oxygen may occur without cyanosis. Cyanosis due to the accumulation of reduced hæmoglobin in the blood is a sign of severe anoxæmia and should be regarded as an indication of danger, even when it has been only transiently present. With the exception of the dramatic coughing up of a foreign body these obstructions do not subside suddenly. Disappearance of cyanosis is ordinarily due to improvement in ventilation, which may prove to be only temporary.

Restlessness is the prime warning of anoxæmia. In a patient with respiratory tract obstruction restlessness must be considered due to anoxæmia unless clearly demonstrated to be caused by some other factor, such as thirst. Sedation must never be given for restlessness in these cases because of the potential aggravation of anoxæmia leading to death.

Anoxæmic restlessness may display itself in the fully wakeful patient, or as inability to sleep, or as waking from sleep. Ventilation may be adequate in a wakeful patient because of increased efforts involving voluntary muscles of respiration. Because these are not available in sleep, ventilation then becomes inadequate, anoxæmia develops and the patient wakes. Repetition of this produces a restless state in a tired patient who is falling asleep. Similar factors operate when obstruction increases during sleep.

Fatigue and inability to sleep provide a very dangerous combination, as a result of which sudden failure of voluntary ventilatory effort may lead at any time to abrupt deterioration and death. Sedatives may produce similar effects by interference with ventilation.

The indications for tracheostomy in mechanical obstruction may be immediate or delayed. Immediate indications are: (*a*) clear evidence of anoxæmia at the time of presentation; (*b*) severe obstruction at the time of presentation without necessarily evidence of anoxæmia; (*c*) obstruction associated with evidence of septicæmia (*H. influenzæ* epiglottitis). Delayed indications are

(*a*) deterioration under observation; (*b*) fatigue or potential fatigue.

Obstruction severe enough to cause gross sternal retraction should be relieved at once, even if there are no overt signs of anoxæmia when the patient is first seen.

Deterioration under observation must include both the onset of anoxæmia and the significant increase in retraction, even without anoxæmia. The former renders tracheostomy obligatory, whereas in the latter case timing of tracheostomy may be related to the final factors of fatigue or potential fatigue. Essentially, these factors may be gauged by prolonged inability to sleep without restlessness.

The administration of oxygen will increase the oxygen saturation in the same way as improvement in ventilation. The fact that it does not alter the degree of obstruction must always be remembered. Its need is a danger signal of the same order as cyanosis, and is ordinarily an indication for relief of the obstruction by tracheostomy.

When tracheostomy is indicated on the above-mentioned grounds, it will be an emergency procedure and should be performed forthwith by the personnel immediately available and in the area in which the patient is situated at that time. A very satisfactory technique is described by Jackson and Jackson (1937).

Management.

Maintenance of Airway.

The actual performance of the tracheostomy is only an incident in the over-all management of the patient. The subsequent preservation of the airway so created is of the utmost importance (Jackson and Jackson, 1937).

Obstruction of the respiratory tract below the tracheostomy by exudate may create great difficulties. This exudate may be thin or may form plugs and even crusts. This applies to the secretional type of obstruction, to cases of laryngo-tracheo-bronchitis, and to other cases in which infection complicates the original cause of obstruction. Management of this secondary obstruction demands that the air passages be kept clear by regular and energetic aspiration with a catheter passed through the tracheostomy tube. Aspiration is aided by the instillation of saturated sodium bicarbonate solution or of normal saline directly into the trachea via the tube. The solution is squirted in with a dropper until the patient begins to cough and to return it and becomes "rattly". The trachea is then cleared with the catheter. The process is repeated until the airway becomes clear. Breathing should then be silent. The instillation of the sodium bicarbonate solution not only aids in dissolving secretions, but also, by stimulating coughing and straining, helps to bring peripheral exudate within range of the catheter.

Humidification of the inspired air by the use of a steam tent or of a "croupette" may help to keep secretions fluid. Detergents such as "Alevaire" may be used at times. The maintenance of adequate hydration is essential.

Aspiration should be performed regularly every 20 to 30 minutes with a recent tracheostomy, and additionally whenever obstruction develops. It may be life-saving for the apparently tired patient who is in fact simply passing into the terminal phase of anoxæmia.

The intervals between aspiration may be lengthened when exudate decreases, as with a retained tube, or if exudate is absent. Apparent absence of exudate may be due to inadequate aspiration. Initially, the amount of exudate cannot be predicted, and care is necessary lest secondary obstruction develops quietly and remains unrecognized until the patient is moribund. Such obstruction should be recognized from the pattern of respiration with expiratory difficulty and emphysema, together with the reappearance of signs of anoxæmia exactly comparable with those occurring before tracheostomy. Observation must remain close, with special attention to restlessness. Sedation continues to be dangerous.

Obstruction may recur also if the tube is dislodged from the trachea before the primary condition subsides. This may be accidental or may occur in the first 24 to 48 hours as a result of swelling of the neck due to surgical emphysema. It is in this period that replacement of the tube is most difficult, usually requiring a clear view of the tracheal opening. Enough air may pass through the displaced tube to give the impression of an effective tracheostomy, but the catheter will not pass beyond the tip of the tube. Lateral X-ray examinations will confirm the position of the tube. Such examinations are indicated whenever there is difficulty with the tube which cannot be solved readily.

Obstruction of the tube itself by crusts should be prevented by regular cleaning of the inner tube.

Decannulation.

The decision to remove the tube with the object of resuming normal laryngeal breathing must clearly be related in timing to the condition for which the tracheostomy was performed.

In laryngo-tracheo-bronchitis in infants and children the obstructive inflammatory swelling in the larynx usually subsides in a few days. By about the fourth day it is reasonable to occlude the tube temporarily by a suitable cork to assess the potential laryngeal airway, allowing for the effect of the tube on the tracheal lumen. If this procedure is tolerated well without evidence of significant obstruction, the tapes are cut and the tube is removed. Removal of the tube leaves a substantial fistula, which, in cases with a recent tracheostomy, may remain widely open for 36 hours or longer. During this time, fistula breathing continues unless the hole is occluded by exudate or, as may happen, by the patient's chin. The outcome of the procedure cannot be predicted or assessed until the patient can be observed with the fistula totally occluded. Very close observation is necessary until laryngeal breathing is fully and satisfactorily resumed. The tube is replaced if obstruction develops.

The period immediately after removal of the tube is of considerable importance. Removal of the tube may be poorly tolerated despite a favourable response to corking. This is more likely in infants and when, for some reason such as persistent tracheo-bronchitis, decannulation is delayed. In these circumstances softening of the tracheal rings in the region of the tracheostomy may develop. Inspiratory collapse of the upper part of the trachea then occurs when the support of the tube is removed. Similar collapse occurs also in cases in which a tracheostomy for non-inflammatory conditions has been performed (Crooks, 1954). Immediate gross obstruction or more delayed difficulties may result.

In the years 1952 to 1957 inclusive, at the Royal Children's Hospital, Melbourne, there were 12 children, other than those with persistent organic narrowing of the larynx such as that due to polypi or laryngeal web, who proved difficult to decannulate after tracheostomy. Two older children whose tubes were retained because of prolonged coma have also been excluded from consideration.

The age distribution of these patients at the time of tracheostomy was as follows: five children were under five months of age and three were aged 6 to 11 months. Only three children were aged 12 to 17 months, and one was two years and three months.

The original condition in seven was primarily inflammatory. In two it was an inhaled foreign body. One tracheostomy followed diagnostic endoscopy, one was performed for micrognathia with respiratory tract obstruction, and one was performed for laryngeal spasm of undetermined origin.

Tracheal collapse was observed in four of seven patients examined to elucidate the difficulty in decannulation. In all seven some degree of subglottic narrowing was also present at some time.

Two patients still have not been decannulated. Of the remaining children, six have been successfully decannulated at periods between 24 days and four and a quarter years after tracheostomy.

Four children have died as the result of attempted decannulation or manipulation of the fistula. One child died suddenly 10 hours after decannulation from occlusion of his trachea by a large plug of mucus. The oldest child, a mongoloid defective, aged two years and three months, whose tracheostomy had been unsatisfactory throughout the seven weeks for which it had been present, became severely anoxæmic and developed cardiac arrest when the tube was removed with the intention of creating a more adequate fistula. In the other two cases death resulted from inability to replace the tube rapidly when obstruction recurred three and a half hours and five hours after decannulation. One of these children was resuscitated by cardiac massage, but died subsequently from the effects of cerebral anoxia.

After the first few weeks the scar tissue, which has developed around the fistula, contracts rapidly once the tube is removed. Instead of remaining open for up to 36 hours, the fistula may be tightly closed within two or three hours. Rapid replacement then becomes virtually impossible, with the results described. For this reason, any attempt at decannulation after the first few weeks should be preceded by excision of the scar tissue down to the trachea. Delayed decannulation is therefore a major procedure to be undertaken only when all the available evidence points to a successful outcome. Observations at bronchoscopy are clearly of great importance. The procedure should not be attempted until the effective lumen (with the tube removed) appears adequate.

If suitable precautions are taken, the ultimate outlook for decannulation should be favourable. As already stated, the longest interval between tracheostomy and decannulation in this group was four years and three months; this was of a boy who was aged 10 months at the time of tracheostomy for acute laryngo-tracheo-bronchitis.

Bigler *et alii* (1954), in a series of 62 infants aged less than 12 months, record the decannulation interval in 14 cases surviving inflammatory obstruction. Decannulation was achieved between 10 and 26 days in nine, and between 33 and 83 days in four. It was not achieved until 455 days in one; the patient was stated to have had laryngeal narrowing due to the infection.

During the waiting period, such children should be managed if possible at home by their parents, to give maximum opportunities for normal development. Such home care is managed well by reasonable parents, provided they have available an efficient sucker and are given adequate support.

Comment.

The criteria by which the need for tracheostomy in mechanical obstruction may be assessed have often been learned by bitter experience. This need not be so provided the importance of restlessness as a sign of anoxæmia and the dangers of fatigue are appreciated.

Awareness of the possibility of secondary obstruction, as stressed by Jackson and Jackson in 1937, and a knowledge of the measures necessary to combat it are of equal importance. The Jacksons recommended bronchoscopy through the tracheal fistula as an additional means to deal with such secondary obstruction. This has not been used in the present group of cases.

The difficulties of decannulating the infant with a tracheostomy have been described in relation to non-inflammatory laryngeal stridor by Crooks (1954), and implied in the figures quoted by Bigler *et alii* (1954). Other reports (Blumenthal and Ravitch, 1957) describe similar difficulties without adequate explanation. It is thought desirable to report further experience, chiefly to support these findings, and to reinforce a warning regarding the complications and dangers provided by the changing behaviour of the fistula after decannulation. The experience described supports the findings of Crooks (1954) regarding ultimate decannulation. With patience and adequate precautions to avoid accidents, the ultimate outlook for decannulation in cases of infants with retained tracheostomy tubes should be good.

The factors rendering decannulation difficult require further investigation.

Summary.

The indications for tracheostomy in childhood are discussed.

The management of tracheostomy is discussed with special reference to the problems of secondary obstruction and of decannulation.

The difficulty of decannulating certain infants is illustrated by a series of 12 patients with retained tubes encountered between 1952 and 1957 in the Royal Children's Hospital, Melbourne. The risks introduced into the decannulation procedure by the changing behaviour of the fistula are emphasized and suitable precautions are advised.

Acknowledgements.

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THE SPREAD OF CANDIDA IN INFANTS AND CHILDREN.

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Increasing attention is being paid in the recent medical literature to the various mycotic infections (Debre *et alii*, 1955; Gerloczy *et alii*, 1956; Torack, 1957). Two basically different groups of mycoses can be differentiated—exogenous and endogenous. The exogenous mycoses, such as histoplasmosis, cryptococcosis, coccidioidomycosis and sporotrichosis, are caused by fungi which are not present in healthy persons. These fungi are pathogenic micro-organisms, and their presence in man indicates a disease process. Endogenous mycoses are caused by fungi which are widely distributed in nature, and which can be detected on the mucous membranes of both sick and healthy persons. Of course, the distinction between the exogenous and endogenous groups is not always sharp.

The endogenous mycoses are of considerable importance in pædiatrics. Dobias recently (1957),[1] reviewing "Moniliasis in Pediatrics", gives 181 references, 101 of them to papers published in the last 10 years. Prevailing opinion associated the increased significance of the endogenous mycoses with the use of certain antibiotics.

Several ubiquitous fungi are capable of inducing mycosis. In an overwhelming majority of the described cases, *Candida albicans* was the pathogenic agent.

C. albicans is the most important species of the genus *Candida*, and is recognized as the most pathogenic amongst them. Other species, such as *C. guillermondi*, *C. parapsilosis*, *C. tropicalis*, *C. pseudo-tropicalis*, *C. krusei*, etc.,

[1] The list of references will be found at the end of the second of these two papers.

can also produce illness in man (Winter, 1955). However, instances have been described in which other endogenous fungi, such as species of *Aspergillus* or *Mucor*, have been the pathogens (Zimmerman, 1950).

The various species of *Candida* can be differentiated only by way of extensive morphological and biochemical investigations (Conant, 1954). They can be readily cultured on any mycological medium. Differential diagnostic value is attributed to clamydospores, which have a thick wall and are produced on corn-meal medium. For complete identification, morphological and biochemical tests are necessary. Occasionally animal pathogenicity tests may be of some use, as *C. albicans* is known to be pathogenic for mice. However, the virulence of different strains for mice is subject to some variation.

The disease caused by this organism is commonly called moniliasis. However, the term candidiasis is preferred by the authors of some of the recent papers.

The published figures concerning the carrier rate of *Candida* and other yeast-like fungi in humans vary considerably from 11% to 81% (Dobias, 1957). It therefore seemed worth while to investigate this problem under present circumstances.

TABLE I.

Candida in the Throat Swabs of Children of Various Age Groups: A, Children Investigated in Budapest; B, Children Investigated in Sydney.

Age.	Number of Children Examined.	Number in whom *Candida* was Present.
New-born:		
A	100	19 (19·0%)
B	191	33 (17·3%)
14 days to 3 months:		
A	54	35 (64·8%)
B	29	4 (13·8%)
3 to 6 months:		
A	66	20 (33·3%)
B	30	6 (20·0%)
6 to 12 months:		
A	130	29 (22·3%)
B	56	16 (28·6%)
Over 1 year:		
A	150	41 (27·4%)
B	130	31 (23·8%)
Total:		
A ..	500	144 (28·8%)
B ..	436	90 (20·6%)

Material and Method.

Five hundred infants and children in Budapest, Hungary (1956),[1] and 436 in Sydney (1957-1958) were investigated for the presence of *Candida*. Of the 500 from Budapest, 100 were healthy new-born infants without any clinical signs of oral thrush, 209 were healthy children from infants' homes and 191 were sick children in hospital. The children in hospital were chosen from certain wards, without regard to their disease. At the beginning of these investigations in Budapest, the oral swabs were investigated by direct smear examination and at the same time cultured on Sabaraud's medium. As the results were about 15% higher with the culture technique, later only this was used. In Sydney, however, 412 cases were investigated by the direct smear method and 14 with the culture technique.

Results.

The results of this investigation are summarized in Tables I to IV.

[1] These investigations in Hungary were carried out in cooperation with Dr. A. Csillag, mycologist of the State Institute of Hygiene, Budapest. Some of the results have been published elsewhere (Csillag, Vince and Simon, 1957, 1958).

The Connexion between Antibiotic Therapy and Fungous Infection.

The connexion between administration of antibiotics and the presence of fungi in man, although often discussed, is still not sufficiently clear. In a former paper (Vince and Csillag, 1956) we postulated as a criterion of generalized candidiasis, positive cultural findings from specimens in which *Candida* is never present under normal circumstances. Blood, cerebro-spinal fluid and urine obtained by catheter were mentioned. Later it was thought necessary to check this question, and the following investigation was undertaken.

TABLE II.

Candida in the Throat Swabs of Healthy Children, Compared with Patients in Hospital: A, Children Investigated in Budapest; B, Children Investigated in Sydney.

Subjects.	Number of Children Examined.	Number in whom *Candida* was Present.
Healthy new-born:		
A	100	19 (19·0%)
B	191	33 (17·3%)
Healthy infants and children:		
A	209	31 (14·9%)
B	34	5 (14·7%)
Total healthy:		
A	309	50 (16·2%)
B	225	38 (16·8%)
Children in hospital:		
A	191	94 (49·2%)
B	211	52 (24·6%)

Sixty infants receiving broad-spectrum antibiotic therapy were investigated. Both blood and a catheter specimen of urine were collected twice a week, from after the fifth day of antibiotic administration. The blood and urine specimens were cultured on corn-meal medium and on Sabouraud's medium. (The culture and the identification of the obtained fungi were performed by Dr. A. Csillag, Institute of Hygienics, Budapest). The results are summarized in Table V.

TABLE III.

Candida in the Throat Swabs of Children in Hospital, Related to Antibiotic Treatment.[1]

Antibiotic Applied.	Number of Children Examined.	Number in whom *Candida* was Present.
Penicillin and/or streptomycin:		
A	110	45 (40·9%)
B	21	5 (23·8%)
Broad-spectrum group:		
A	49	28 (57·1%)
B	106	29 (27·3%)

[1] The patients were all receiving antibiotic therapy of some days' duration, or had completed a course of therapy within the last three days; A, children investigated in Budapest; B, children investigated in Sydney.

Discussion.

Before the foregoing results are discussed, the two methods used in the investigations must be compared. The figures obtained by applying the culture technique are usually higher. Marples and di Menna detected *Candida* in 18·3% of the subjects examined by direct smear, and by culturing the mouth washings in 33·5% of children and 50·4% of adults respectively. Lilienthal obtained 37·0% of positive results in swabbings from the gums and 47·7% by culturing the saliva. Our preliminary investigations, as mentioned, yielded 15% higher figures with the culture

technique. The direct-smear method has the advantage of technical simplicity, but it does not allow the proper differentiation of the various yeast-like fungi. On the other hand, as most of the yeast-like fungi found in human carriers are *C. albicans* (Lilienthal, 1950; Wegmann, 1954), and the others appear to be potential pathogens as well, for practical purposes the direct-smear method seems to be sufficient.

Concerning the results summarized in Tables I and II, the close agreement of positive findings between new-born and healthy children in Sydney and those in Budapest is remarkable. This agreement in the healthy children makes more interesting the divergence in the children

TABLE IV.

Time of Appearance of Candida Albicans in the Throat Swabs of New-born Infants.[1]

New-born Infants Examined.	Day of Appearance of *Candida*.	Number of Positive Results.
100	4 to 6 7 to 9 10 to 14	8 5 6
Total ..	.. ..	19

[1] These investigations were carried out in Budapest, at daily intervals, on all infants.

in hospital. The difference between 49·2% and 24·6% cannot be fully explained by the two methods used. The data concerning the positive findings in the new-born and healthy group agree well with the earlier findings of Marples and di Menna from New Zealand (1952), and with that of Anderson *et alii* from the U.S.A. (1944). The earlier Australian data of Lilienthal (1950) are somewhat higher. The percentage of positive findings in the children in hospital is only slightly higher in Sydney than in the healthy or new-born group. On the other hand, in Budapest the incidence in the same group was twice as high. This is astonishing, since the proportion of children treated

TABLE V.

Candida Albicans in the Blood and Urine of Infants, after More than Five Days' Broad-Spectrum Antibiotic Treatment.[1]

Biological Material.	Number of Infants.	Number of Specimens Cultured.	Number of Positive Results.	
			Infants.	Specimens.
Blood ..	60	110	3	6
Urine ..	60	156	19	30

[1] This investigation was carried out in Budapest (1956).

with broad-spectrum antibiotics was significantly higher in Sydney, where the investigations were carried out almost entirely under warm, humid weather conditions favouring the spread of *Candida* (Dobias, 1957). A possible explanation may lie in the fact that the pædiatric hospitals in Budapest were overcrowded at the time, and there was also a relative shortage of nursing staff. It seems reasonable to arrive at the conclusion that the hygienic and nursing conditions in a hospital are more important factors than antibiotics in influencing the occurrence of yeast-like fungi.

The data given in Table IV have the interesting feature that no fungi were detected in new-born infants before the fourth day of life. This appears to contradict the possibility of infection from vaginal mycosis at birth. It seems more likely that infection occurs later. This again underlines the importance of the hygienic conditions.

Table V proves that antibiotics can influence the spread of fungi within the body. Under normal circumstances no fungi could be detected in the urine. Ballowitz and Schafer, in a control series of 800 children, were unable to culture fungi from the urine. They found fungi in the urine of 16 infants and children out of a series of 120 after administration of antibiotics. Of the infants listed in Table V, only three suffered from generalized candidiasis. These three yielded positive blood cultures as well. In a further three or four instances it was possible that the appearance of *C. albicans* in the urine was connected with the deteriorating clinical picture, but in most cases the findings appeared to have no clinical significance. This points to the need for the utmost caution in evaluating the laboratory findings concerning these ubiquitous fungi.

It seems that under present circumstances a relatively large proportion of infants and children are harbouring *C. albicans* or other yeast-like fungi on their mucous membranes. Prolonged administration of antibiotics promotes the appearance of fungi in the urine; this probably does not mean disease in itself, but should be regarded as a signal indicating the possibility of mycosis.

Summary.

Five hundred infants and children in Budapest, Hungary, and 436 infants and children in Sydney were investigated for the presence of *Candida*.

The percentages of positive findings in the new-born and healthy children were in close agreement in both groups. The incidence of fungi in the children in hospital was twice as high in Budapest as in Sydney. The importance of hygienic conditions and nursing facilities is stressed.

Blood and urine were investigated in a series of 60 infants who had received more than five days' broad-spectrum antibiotic treatment. Three infants yielded positive blood cultures; all of them were suffering from generalized candidiasis. From 19 infants, 30 positive urine cultures were obtained. In the majority of these, no clinical significance could be attributed to these findings.

It seems that prolonged administration of antibiotics can influence the spread of the fungi within the body, and that it promotes their appearance in the urine. These findings in themselves probably do not signify a disease process. Positive blood cultures, on the other hand, seem to have always diagnostic significance.

GENERALIZED ENDOGENOUS MYCOSIS IN CHILDHOOD.

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THE clinical picture and significance of the generalized infections caused by "thrush fungi" were recognized and well described by the pædiatricians of the nineteenth century (Valleix, 1838; Parrot, 1877). Later, it appeared that the medical literature associated the concept "systemic mycoses" only with the exogenous fungal infections. It was believed that the endogenous fungi, the candidas and others, were mainly responsible for the superficial skin and mucous membrane thrush. In recent years new interest has been focused on the question.

Convincing data (Gerloczy *et alii*; Torack, 1957) suggest that not only is there a quantitative increase in endogenous mycoses, but more severe, generalized forms are reappearing. Candida endocarditis, meningitis and septicæmia have been reported recently (Gausewitz *et alii*, 1951; Huppert *et alii*, 1953; Wybel *et alii*, 1952; Zimmermann, 1950; Burry, 1957; Vince and Csillag, 1956). Most of these cases have been diagnosed on post-mortem evidence, so that if similar cases had occurred in previous years, the pathologists, who were well aware of the significance of the fungal infections (Reye, 1941), would hardly have failed to detect them. The prevailing opinion

associates the growth in number and significance of the endogenous mycoses with the use of certain antibiotics.

The purpose of this paper is to discuss the problem of generalized endogenous mycosis from the pædiatrician's point of view. I shall not refer to the subject of skin or mucous membrane moniliasis.

I have had the opportunity of following the progress of nine patients with generalized endogenous mycoses. Eight of them were studied in Budapest, Hungary, between 1954 and 1956; they were under my care in the first Pædiatric Clinic of the University of Budapest. Reports of three of these cases have been published previously (Vince and Csillag, 1956). The ninth patient was examined in Sydney (1957), and was under the care of Dr. D. G. Hamilton. The main features of the nine histories are summarized in Table I.

As is seen in this table, the clinical picture was very varied. It is well known that the generalized endogenous mycoses are usually secondary to some other pathological process. It seems that the primary disease substantially influences the whole course of the secondary mycoses. It appears that the primary process, by causing some sort of *locus minoris resistentiæ*, almost determines the sites of invasion for the fungi, and also may determine which organs or systems are most likely to be affected by the fungal septicæmia. This explains why pulmonary involvement is such a common finding, since recurrent respiratory tract infections are the most common precursors. Mycotic gut perforation following bacterial enteritis, and mycotic meningo-encephalitis following intracranial hæmorrhages and hydrocephalus, can be understood on this basis. The presenting symptoms are those of acute or subacute septicæmia, not differing from other septic diseases of infancy.

In some instances the relative absence of toxic symptoms was an interesting feature. The patient's behaviour and appetite were sometimes quite satisfactory, in astonishing contrast to the high fever and protracted disease.

The laboratory findings also varied to a large extent. In some cases, more or less marked anæmia was noted. Sometimes slight leucocytosis with relative neutrophilia was encountered. This hæmatological change did not appear characteristic of candidiasis, and was probably related to the preceding illness.

The serum protein patterns of six of the infants discussed have been determined by paper electrophoresis. Two infants had normal patterns, one had constant hypogammaglobulinæmia, two produced a paradoxical reaction. Usually, after prolonged or repeated infections, a rise in the gammaglobulin level occurs. However, in these two instances, a marked fall in gammaglobulin level was noted. The ninth child, who was examined in Sydney, had or developed agammaglobulinæmia.

Diagnosis.

Diagnosis of the endogenous mycoses is often difficult. Its symptoms, as has been stressed above, are not characteristic of fungal infection, so it is not possible to differentiate the disease by mere clinical appearance. The pædiatrician should consider the possibility of mycosis, and it is the pathologist's task to confirm the diagnosis by way of mycological investigations.

Concerning the question of laboratory diagnosis, one must keep in mind that the agents of endogenous mycoses are ubiquitous fungi. In the previous paper the presence of fungi has been shown in 17·3% to 19·0% of healthy, new-born infants, in approximately 14·9% of healthy infants and children, and in 24·6% to 49·2% of infants and children in hospital. Diagnostic value can be attributed therefore only to the isolation of fungi from sites where they are not normally detected. Thus the isolation of *Candida* from the skin, mucous membranes, sputum, fæces and urine (not obtained by catheterization) has very little diagnostic value. The detection of *Candida* strains in blood, cerebro-spinal fluid, urine collected by way of sterile catheterization and secretions obtained bronchoscopically has significance; but at the same time it must be emphasized that the detection of fungi in the body fluids mentioned does not necessarily imply candidiasis. As was shown in the previous paper, it was possible to detect *Candida* in the urine obtained by catheterization in 19 infants out of a series of 60 after treatment with broad-spectrum antibiotics, and this finding in the great majority of cases seemed to have no clinical significance.

In my opinion the following criteria should be fulfilled before a diagnosis of candidiasis is made: (i) the presence of clinical symptoms; (ii) the absence of other bacteriological or virological findings which could explain the clinical picture; and (iii) the isolation of fungi from one or more of the body fluids mentioned above.

As contamination occurs rather easily, the laboratory findings are convincing only if the same fungus is isolated at least twice in pure culture. In fungal septicæmia the organism appears periodically in the blood; hence one negative result does not exclude the diagnosis of generalized mycosis. The investigations should be repeated three or four times.

The serological reactions and cutaneous tests do not offer much help for the diagnosis. They are of doubtful specific value. Because infants often fail to produce antibodies, the results of cutaneous tests may remain negative; on the other hand, they are often positive in healthy persons (Carpenter, 1952; Conant, 1954; Erdos, Szekely and Vince, 1955).

Pathogenesis.

The fungi causing endogenous mycosis belong to the group of facultative or potentially pathogenic microorganisms. This type of agent is capable of causing illness only when the virulence of the microorganism happens to increase and/or the resistance of the host decreases.

Let us consider the data concerning the influence of antibiotics on the virulence of fungi. Much experimental work deals with the in-vitro effect of certain antibiotics on the growth of fungi. The results are contradictory. More convincing are the results of animal experiments. They prove that mice succumb more quickly when they receive *C. albicans* and some broad-spectrum antibiotic intraperitoneally than do those in a control group receiving the same fungi alone (Seligmann, 1953; Csillag, 1956). *C. albicans* is pathogenic for mice—that is, every strain is able to cause illness in mice if it is present in sufficient quantity. Therefore, in my opinion, the animal experiments described above do not prove that antibiotics have a direct promoting effect on the virulence of fungi. It is possible that antibiotics influence only the factors concerned in fungal growth. The pathogenicity to mice of strains of *C. albicans* isolated from patients suffering from generalized candidiasis did not show significant differences compared with strains isolated from healthy infants (Csillag and Vince, 1956).

There are several theories which attempt to explain the mechanism by which antibiotics influence the growth of endogenous fungi. They may be briefly discussed as follows.

1. The physiological equilibrium of the normal microflora of the host is upset. The microorganisms sensitive to the applied antibiotics are destroyed. It is suggested that this allows the rapid overgrowth of fungi, (*a*) because these are resistant to the antibiotics concerned, (*b*) because the "fungistatic" effect of the bacteria is cancelled, (*c*) because the bacteria do not utilize the nourishment, and (*d*) because the destroyed bacteria are in themselves excellent media for fungi.

2. Certain antibiotics destroy the normal coliform flora of the gut, which has an important part in the synthesis of certain vitamins, such as vitamin B complex and vitamin K. As a consequence, the developing hypovitaminosis diminishes the resistance of the mucous membranes, a fact which favours fungal invasion.

3. Earlier mycotic foci, or perhaps some antibiotics of fungal origin, could have a sensitizing effect on the host, favouring a rapid spread of pathogenic fungi.

4. The pH of the mucous membrane of the mouth changes towards acidity, a condition which is thought to be more favourable for the settlement of fungi.

TABLE I.

Case Number, Patient's Sex and Age. (Months.)	Primary Illness.	Antibiotics Adminis-	Bacteriological Findings.							Mycological Findings.				Treatment.	Result.
			Mycobacterium Tuberculosis in Gastric Contents.	Attempted Blood Culture.	Attempted Culture of Urine Catheter Specimen.	Attempted Culture of Cerebro-Spinal Fluid.	Throat Swab. (Predominant Organism.)	Pathogenic Organisms in Fæces.	Response to Widal Test.	Fungal Elements in Blood. (Direct Film.)	Fungi Grown on Blood Culture.	Fungi Grown on Urine Culture.	Fungi Grown from Other Sources.		
A., F., 18	R.U.R.I.[1], pneumonia, cystopyelitis.	P., Str., Chl., Ot., Clt.	No growth.	No growth.	No growth.	No growth.	*Pseudomonas pyocyanea.*	—	Negative.	+	*C. albicans.*	*C. albicans.*	—	P.o.b.[2]	Improvement.
B., F., 6	R.U.R.I., pneumonia.	P., Str., Ot.	No growth.	No growth.	No growth.	No growth.	*Proteus, Ps. pyocyanea.*	—	Negative.	+	An unidentified species of *Candida.*	—	—	Symptomatic.	Improvement.
C., F., 1	Cleft palate, pneumonia, malnutrition.	P., Str., Ot.	No growth.	No growth.	No growth.	—	—	—	—	+	*C. albicans.*	—	Bronchial secretion: *C. albicans.*	P.o.b., "Multergan".	Death.
D., F., 8	Enteritis.	Chl., Ot.	—	—	No growth.	—	No growth.	*Escherichia coli* O.III B4.	—	—	—	*C. albicans.*	Fæces and secretion of abdominal cavity: *C. albicans.*	P.o.b.	Improvement.
E., F., 18	Intracranial Hæmorrhages, hydrocephalus, R.U.R.I.	P., Str., Chl., Clt.	No growth.	No growth.	No growth.	No growth.	No growth.	—	Negative.	+	*C. tropicalis.*	*C. tropicalis.*	Cerebro-spinal fluid: *C. tropicalis.*	P.o.b., gamma globulin.	Improvement.
F., M., 12	Congenital heart failure, pneumonia, R.U.R.I., enteritis.	P., Str., Ot.	No growth.	No growth.	No growth.	No growth.	*Proteus.*	—	—	+	*Torulopsis glabrata.*	*C. albicans* and *T. glabrata.*	Bronchial secretion: *T. glabrata.*	P.o.b., gamma globulin.	Improvement.
G., M., 8	Otitis media, R.U.R.I., enteritis.	P., Str., Chl., Clt.	No growth.	No growth.	No growth.	—	*Staphylococcus albus.*	—	Negative.	+	*C. pseudotropicalis.*	—	Throat swab: *C. albicans*; bronchial secretion: *C. pseudotropicalis.*	Gamma globulin.	Improvement.
H., F., 5	R.U.R.I., pneumonia.	P., Str., Ot., Clt.	No growth.	No growth.	No growth.	—	*Staph. albus.*	—	—	+	*C. albicans.*	*C. albicans.*	—	P.o.b., gamma globulin.	Improvement.
I., M., 9	R.U.R.I., bronchiectasis, agammaglobulinæmia.	T.	—	No growth.	No growth.	—	—	—	—	—	—	—	Throat swab: *C. albicans.*	"Mycostatin", gamma globulin.	Death.

[1] R.U.R.I. = Recurrent upper respiratory tract infection.

[2] P., penicillin; Str., streptomycin; Chl., chloramphenicol; T., tetracycline; Ot., oxytetracycline; Clt., chlortetracycline.

[3] P.o.b. = Paraoxybenzoic acid ester.

5. Certain antibiotics may have a direct growth-promoting effect. This assumption has already been mentioned.

Perhaps all these factors may have some significance, but the elimination of the sensitive microflora seems to be decisive. This indicates why broad-spectrum antibiotics are the most likely cause of fungal spread.

In view of the foregoing discussion, these factors can provide sufficient explanation for the results of experimental candidiasis in mice. Since the disease in mice occurs with certainty when the necessary number of micro-organisms is present, it will clearly develop earlier if a substance capable of hastening the multiplication of fungi is administered in addition. If the same factors alone could explain the *Candida* infections in humans, this should have been an everyday finding. A significant percentage (24·6% to 49·2%) of infants and children in hospital harbour fungi in their mouths; in the investigated series, the fungus appeared in the urine of every third infant after more than five days of broad-spectrum antibiotic treatment; yet very few of these patients develop mycoses. There must be some additional factor which decides whether these facultative pathogenic fungi, whose growth has been hastened by the administration of antibiotics, are to produce pathological changes or not. It seems clear that the actual state of the defence mechanisms of the host must be this decisive factor. It is well known that the facultative pathogenic agents cause illness only in exhausted, weakened individuals; yet it seems that in recent years insufficient attention has been paid to this side of the question.

Torack, making a distinction between surface and invasive fungal lesions, suggests that the "former occurs when antibiotic therapy alone is employed; the latter is associated with combined antibiotic and steroid therapy". It appears that in children, especially in infants, a severe, long-lasting or recurrent disease can produce depression of the immunological mechanisms similar to that produced by steroid therapy, thus converting the surface fungal thrush to invasive fungal septicæmia. Without discussing the contradictions concerning the significance of gamma-globulin levels in relation to the immunological state of the organism, I would mention only that the hypogammaglobulinæmia or agammaglobulinæmia found in some of the cases described could have been the symptoms of this immunological depression.

Treatment.

The therapy of endogenous generalized mycosis is necessarily complex. On the one hand adequate antimycotic drugs such as "Mycostatin" (nystatin) or "Paraben" (paraaminobenzoic acid) should be applied, and on the other hand symptomatic therapy should be directed to improving the patients' condition by all possible means. The administration of gammaglobulin seems to be justified.

The question of antibiotic therapy can cause some concern. Usually, if endogenous mycosis is diagnosed, antibiotic treatment should be discontinued. However, a mycotic infection may complicate an unresolved bacterial infection, frequently staphylococcal (Hottinger, 1956), and in those circumstances the form of antibacterial treatment should be chosen with regard to the mycotic infection. No tetracyclines or chloramphenicol should be used, but if necessary penicillin, streptomycin or erythromycin or their combinations may be used. The last-mentioned group only slightly influence the normal coliform flora, and so are probably less hazardous as accelerators of mycotic superinfection. Of course, antimycotic treatment must be applied simultaneously.

Summary.

A tabulated short history of nine children suffering from generalized endogenous mycosis has been presented.

The problems of the diagnosis and pathogenesis of endogenous mycosis have been discussed in detail.

A significant percentage of infants and children harbour yeast-like fungi on their mucous membranes, as was shown in the previous paper.

It is considered that administration of antibiotics plays an important role in promoting the growth of fungi and can cause their spread within the body; but the decisive factor in the occurrence of secondary mycosis may be the lowering of the patient's resistance by lasting or recurrent infections.

The need for complex therapy has been stressed.

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NORMAL PREGNANCY — A CUSHING'S SYNDROME.

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NORMAL PREGNANCY has many features in common with Cushing's syndrome. Although the cases in Cushing's original series (1932) were mainly associated with basophil adenomata of the pituitary, it is now realized that the majority are associated with hyperplasia of the adrenal cortex.

The symptoms and signs, with their frequency as reported by Plotz, Knowlton and Ragan (1952) from the Presbyterian Hospital, New York, are as follows:

Obesity	97%
Hirsutism	73%
Purple striæ	60%
Hypertension	84%
Amenorrhœa, oligomenorrhœa, impotence in the male	86%
Plethoric appearance	89%
Mental symptoms (major 24%, minor 43%)	67%
Poor wound healing or severe infection	42%
Weakness and backache	83%
Acne, skin pigmentation or other rash	82%
Purpura or easy bruisability	60%
Ankle œdema	60%
Headache	58%
Neurological symptoms or signs	39%
Polydipsia or polyuria	39%
Virilism	9%
Exophthalmos	6%
Eosinopenia (below 100 eosinophils per cubic millimetre)	79%
Osteoporosis of the spine	83%
Osteoporosis of the skull	60%
Altered glucose tolerance curve	94%

Most of the published evidence of adrenal cortical hyperactivity in normal pregnancy has been laboratory-inspired. Venning (1946) showed that there was an increased urinary excretion of glycogenic corticosteroids during normal pregnancy, with a return towards normal levels at term. Robinson *et alii* (1955) showed that there was a rise in the plasma corticosteroid level, but stated that the return to normal took six weeks from the date of delivery. Gemzell (1953) showed that the blood level of 17-hydroxycorticosteroids rose to four times the normal during pregnancy and to seven times the normal in the few days following delivery. Aldosterone excretion has been shown to rise throughout pregnancy (Venning and Dyrenfurth, 1956; Venning *et alii*, 1957).

Method of Study.

Clinical evidence of similarity was sought in a special study of 116 primigravidæ. These were consecutive patients who booked in at both the Queen Victoria Maternity Hospital and the Queen Elizabeth Hospital, the the only proviso affecting acceptance being that the pregnancy should not be more advanced than 14 weeks. More than 1400 clinical examinations were carried out by the same observer (L.O.S.P.) during the 116 pregnancies. Blood glucose curves were prepared for 98 women, while special blood examinations, consisting of red and white cell counts with differential leucocyte counts and an absolute eosinophil count, were made on an average of six times per pregnancy. The blood glucose tests were commenced at 8 a.m., while the other blood specimens were always taken between 9 and 10 a.m. and examined within six to eight hours by the same technician throughout the whole study.

Consideration of Individual Symptoms and Signs.

In the following discussion, the percentages in parentheses refer to the incidence in Cushing's syndrome.

Obesity (97%).

Previous clinical studies (Sheldon, 1949) leave us in no doubt that pregnancy *per se* is a direct cause of obesity. As judged by increased fat deposits and excessive weight gain, obesity is known to commence early or late in pregnancy or in the puerperium. Sheldon made the observation that it was more common after the birth of male babies.

Weight gain in pregnancy, with all the valuable studies and contributions of the past, is still far from being clear of interpretation in each individual. The two main causes are water retention and fat. It is the former which has received most attention and glamour in recent years. Although in many cases water retention would appear to be the main cause, as is subsequently proved by weight loss when sodium intake is reduced together with a return to the pre-pregnancy weight within the very early puerperium, nevertheless this fails to explain clinical findings in a high percentage of cases. It is often noted that a tendency to obesity begins during the pregnancy in some women and causes excessive weight gain, even between the twentieth and thirtieth weeks.

A study of residual weight changes at approximately six months after delivery in this series of primigravidæ shows that 70% of women were heavier after childbirth. Some patients were eliminated because a second pregnancy had begun at this time and others because accurate weight records were not available at the six months' post-partum period, whilst a few could not be traced; 81 of the original 116 were thus available for study.

Two women weighed exactly the same six months after delivery as they did just prior to conception. Twenty-two lost weight, three of them having lost 17, 21 and and 24 pounds respectively; the great majority were lighter by a few pounds only. Fifty-seven women gained weight (this represents 70%); five of these were heavier by more than two stone, while the two greatest gains were 34 and 37 pounds respectively.

No detailed investigations were made of each woman to find the relationship of the weight variations to lactation, amenorrhœa, environment, diet or other factors. Several of those who gained more than 14 pounds were interviewed, and the majority were anxiously trying, with much difficulty, to lose weight.

Maternal obesity is ill-understood and constitutes a fascinating study. Granted, obesity in the final analysis must depend on food intake (Newburgh and Conn, 1944); yet the level at which the intake will lead to obesity must depend on pluriglandular and other individual

factors. There is little doubt that the adrenal cortical hyperactivity of pregnancy is responsible for setting in motion a chain of events leading to increased fat deposition in some women, just as in Cushing's syndrome. Sheldon (1949) stressed the familial aspect when he showed that maternal obesity was twice as common in the mothers of fat women as in the mothers of his non-obese group. Mullins (1958) showed a close relationship between obesity and low intelligence. The exact cause of obesity in an individual woman is therefore probably a mixture of factors, even though therapy must begin with a controlled intake.

Further clinical studies are required, and are being made, on this complicated subject of maternal obesity. Meanwhile we may accept the fact that there is a relatively high incidence of true obesity, central in distribution, during and after normal pregnancy, just as we accept the same type of obesity in Cushing's syndrome whether "sub-clinical" or established.

Hirsutism (73%).

Minor degrees of hirsutism were recorded as developing in 62 pregnancies of this series, or 53%.

Purple Striæ (60%).

Purple striæ simply mean active striæ, in contrast with the pearly-white appearance of the old non-active state. In pregnancies of primigravidæ, active striæ may commonly be seen on the breasts, abdominal walls, hips and thighs, and very occasionally on the arms. In this study they were found on the breasts in 60% of women, on the abdomen in 60% and on the hips in 53%.

Detailed measurements of the abdominal and hip circumferences, taken at each visit and related to the onset of striæ, produced conclusive evidence that there was no direct relationship between the amount of skin stretch and striæ formation.

When several levels of percentage stretch of the abdominal wall were examined, the findings were as follows:

When stretching of the abdominal wall was less than 15%, striæ developed in 83%. When stretching of the abdominal wall varied from 15% to 29%, striæ developed in 42%. When stretching of the abdominal wall was 30% or more, striæ developed in 33%.

These findings are not consistent with the theory that stretching alone causes striæ. It can also be shown that chance was not operating. The only explanation lies in the acceptance of each woman's having her own "striæ factor". Those with the highest concentration develop their striæ at the lowest levels of stretch, while those with the lowest concentrations are able to resist the greatest percentages of stretch without developing striæ. In the hip striæ study, 25% developed purple striæ before any increase in measurement had occurred at all.

It is thus clear that striæ in pregnancy have approximately the same incidence as quoted for Cushing's syndrome. Clinical evidence is now available showing an intimate relationship between striæ and hypercortisonism (Poidevin, 1959).

Hypertension (84%).

Fifty-nine patients (51% in this series) developed some relative rise in blood pressure during pregnancy, as shown in Table I.

This is not the occasion for any form of discussion on hypertension in pregnancy. Factual evidence showed that 51% of patients developed some relative rise during pregnancy.

An incidental finding was that 87% of women with toxæmia of pregnancy had striæ, whilst only 53% of the non-toxæmic women had them. This tempts one to suggest a closer relationship between toxæmia of pregnancy and hypercortisonism.

Plethoric Appearance (89%).

This sign was not statistically observed in my study. However, in the lesser degrees it is commonly seen, and often in association with the minor degrees of "moon face" or "tomato face" of late pregnancy.

Mental Symptoms (67%).

The mental symptoms quoted by Plotz *et alii* (1952) ranged from irritability and depression to hysteria and suicidal states. It was not practicable to attempt the recording of such symptoms in this series. The emotional tenor of most women is subject to considerable fluctuations throughout the reproductive years, and greater variations than usual in pregnancy are commonly accepted as due to the not inconsiderable physiological and psychological rearrangements required by pregnancy. Pregnancy psychoses vary widely according to each individual's response to the stresses of pregnancy and the puerperium. In most cases these psychotic disturbances are short-lived and recede as the pregnancy is left behind.

TABLE I.

Rise in Blood Pressure in 59 Cases.

Rise. (Mm. of Mercury.)	Systolic.	Diastolic.
10 to 20	34	43
21 to 30	18	9
31 to 40	4	4
40 and over ..	3	3
Total ..	59	59

Poor Wound Healing or Severe Infection (42%).

The few surgical wounds made in this series during pregnancy concerned those for the removal of striæ gravidarum for histopathological study. Whether these wounds were on the breasts, abdomen or hips, it was commonly found that healing was poor and frequently by second intention over several weeks. One laparotomy wound at the twenty-fourth week of a pregnancy broke down on the ninth post-operative day, although the healing appeared satisfactory on the eighth day when the sutures were removed.

Much evidence is available to show that fibroblastic reaction is inhibited and even suspended during the administration of cortisone or its derivatives and ACTH, and also in other hypercortisone states (Creditor *et alii*, 1950; Alrich *et alii*, 1951; Baxter *et alii*, 1951; Conway and Stark, 1951).

There were no severe infections in this study.

Weakness and Backache (83%).

These two symptoms are commonly complained of during pregnancy, particularly the latter, both early and late in pregnancy. No special factual observations were made in this study.

Acne, Skin Pigmentation or Other Rash (82%).

Skin pigmentation of the nipple area and the linea nigra is so universal in pregnancy as to be accepted as normal in more than 90% of women. Facial pigmentation or chloasma occurred in this series in 24 women, or 21%.

Acne, usually of mild degree, and consisting of a few pimples on the forehead and round the mouth and chin, is a most frequent finding in pregnancy. Women rarely complain, accepting it in the same way as they do the few pimples which frequently accompany menstruation, and manage it cosmetically. This sign of adrenal cortical hyperactivity has been, and will continue to be, overlooked unless particular note is taken. In this study acne occurred in 88 women, or 76%.

Purpura or Easy Bruisability (60%).

No special note was made of this sign in the present study. However small purpuric spots are frequently found on the skin of the hands and forearms and trunk if searched for particularly, while bruising is not infrequently noticed in pregnancy.

Ankle Œdema (60%).

This sign has a high frequency in pregnancy, and although it has several explanations particular to pregnancy, nevertheles it is a sign common to both states being considered.

Headache, etc.

Headache, neurological symptoms and signs, polydipsia or polyuria, virilism and exophthalmos all have their particular incidences in pregnancy, and as no particular study was made of them on this occasion, no further comment is required.

Eosinopenia (79%).

Eosinopenia (eosinophils numbering less than 100 per cubic millimetre), even with the variable factors which influence it, is nevertheless considered a reliable index of corticosteroid activity (Prunty, 1950). In this study, eosinopenia to this degree occurred in 107 women at some stage during their pregnancy. This is equivalent to an incidence of 92%. (Sequestrated blood was used and examined in the counting chamber within six to eight hours in every case.)

Osteoporosis (*Spine* 83%, *Skull* 60%).

In order to determine the incidence of osteoporosis in pregnancy, considerable radiological exposure would be required. This was considered unjustifiable. That osteoporosis does occur in pregnancy is well established, and possibly it accounts for some of the backaches encountered. It almost certainly is responsible for the occasional spontaneous rib fracture, which may be precipitated by such simple acts as coughing or sneezing or even turning in bed. These rib fractures are more common than is generally appreciated, and should be thought of when pain in the chest in middle or late pregnancy is being investigated, even though there is no history of trauma. In 1956 Savage reviewed the literature, and was able to find only 13 cases of stress fracture of the ribs in pregnancy; to these he added three further case reports. The true incidence is far in excess of this impression, which fact can be explained only by the failure, firstly to diagnose the condition, and secondly to report such cases.

Altered Glucose Tolerance (94%).

Ninety-eight women had blood glucose readings taken half-hourly for a three-hour period after the oral ingestion of 50 grammes of glucose. These tests were conducted between the thirty-fourth and thirty-eighth weeks of pregnancy by the use of the highly accurate modification of Roman (1959, in publication) of the method of Hazelwood and Strookman (1939).

In 61 women there were varying degrees of delay in return to the fasting blood sugar level by the end of two hours. Thus 65% of this series showed altered glucose tolerance. Incidentally, a very close relationship was shown between the occurrence of striæ and delayed glucose tolerance, which latter sign is well accepted as a hypercortisone effect.

Conclusion.

Clinical evidence is presented which emphasizes the similarity between normal pregnancy and Cushing's syndrome. Already there is much supporting laboratory evidence.

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Reports of Cases.

STAPHYLOCOCCAL PNEUMONIA TREATED WITH "SPONTIN".

By J. C. H. MORRIS,
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THE patient, Mr. A., was aged 66 years. He had had no previous serious illnesses or chest infections, and was a farmer in good physical condition. He was first examined on May 20, 1958, because on each of the previous few nights he had woken feeling very hot and literally bathed in perspiration. He had no cough, and his only other complaint was that his appetite was poor. Examination of the patient at this time revealed that his temperature was normal, and there were a few coarse crepitations at the bases of both lungs, rather more obvious on the left side. He weighed 9 st. 12 lb., and he did not appear very ill. He was given no specific treatment at that stage, as the cause of his night sweats had not been determined.

He was examined again two days later, when his temperature was 99·6° F., and the signs at both lung bases were more marked. He was given penicillin injections (300,000 units of crystalline penicillin and 900,000 units of procaine penicillin) once a day, but showed no improvement after three days. Chest examination now suggested that an effusion was developing at the base of the right lung, so on May 25 he was admitted to a private hospital.

Because there had been no clinical response to penicillin, and pending the result of sputum culture, chloramphenicol was administered in a dosage of 250 mg. four times a day. A chest X-ray film confirmed the probable presence of fluid at the base of the right lung, the left costophrenic angle was also hazy and all the lung markings appeared "fluffy".

Because of the deterioration in his general condition, treatment with 500,000 units of crystalline penicillin twice

a day was commenced, but had to be ceased after a few days because of a generalized skin eruption. At this stage the result of the sputum culture became available, and miscellaneous organisms were grown, all insensitive to penicillin, streptomycin, the tetracyclines, chloramphenicol and erythromycin.

The patient's condition was rapidly becoming worse; he was becoming very dyspnœic and at times cyanotic. The night sweats persisted, and were like the profuse sweating sometimes seen in Hodgkin's disease. The chest signs by now showed definitely the presence of a right basal effusion, and on June 4, 500 ml. of straw-coloured fluid were aspirated from the right lower quadrant of the chest. The deposit from this fluid consisted mostly of endothelial cells and lymphocytes. No organisms were seen, and culture produced no growth (including culture for *Mycobacterium tuberculosis*). Another culture of his sputum at this time produced staphylococcus and monilia, both again insensitive to all the antibiotics listed previously.

After the chest aspiration, the patient's severe sweating attacks were temporarily ameliorated, but did not cease. A further chest X-ray film showed the base of the right lung to be now clear; but marked haziness had now developed over the upper two-thirds of the right lung field, but not including the apex. On the left side there was marked parahilar haziness.

In view of the lack of response to the antibiotics, and in spite of the results of sputum culture, in the hope of some in-vivo response, treatment with erythromycin (250 mg. four times a day) was begun on June 6, and on June 8 novobiocin (250 mg. four times a day) was added. With the administration of novobiocin, there was a rapid improvement in his condition, his temperature fell to normal within 36 hours and his night sweats ceased.

He progressed satisfactorily over the next few days, and on June 14 erythromycin was ceased, novobiocin being continued. At this juncture, signs at the base of the left lung were more marked, and his chest X-ray films showed no striking changes.

Over this period he was apparently holding his own quite well, but on June 16 his condition suddenly became worse, and he began to develop an expiratory wheeze in the left side of his chest, which was thought to be due to compression of the left main bronchus by the parahilar lymph nodes. His abdomen became very distended, although bowel sounds were still audible. At this stage he was obviously gravely ill. He was examined in consultation by Dr. D. Nathan, who suggested that an attempt be made to obtain a supply of the new antibiotic ristocetin (produced by Abbott Laboratories and marketed under the name of "Spontin").

A limited supply of 12·5 gm. of this drug was kindly dispatched by air by the Melbourne representative of Abbott Laboratories, and the patient was given 1·5 gm. dissolved in 500 ml. of dextrose solution (5% in water) by the intravenous drip method, the infusion taking 45 minutes to run into the vein. The patient's weight at this time was approximately 110 lb. (50 kg.). By the following morning there was an obvious improvement in the patient's condition, and this continued dramatically over the next few days. At this stage prednisolone therapy was commenced (60 mg. in four divided doses on the first day), as it was thought that the ristocetin was controlling the infection adequately and his condition had caused so much concern. The dosage of ristocetin given this case was as follows:

	Morning	*Evening*
June 18	—	1·5 grammes
June 19	1·5 grammes	1·5 grammes
June 20	1·5 grammes	1·25 grammes
June 21	1·25 grammes	1·0 gramme
June 22	1·0 gramme	1·0 gramme
June 23	1·0 gramme	Ceased

By June 23, the patient was remarkably better, his meteorism had subsided, he was beginning to eat and he felt well in himself. He developed a slight cough and produced a little yellowish sputum, and his chest signs were greatly diminished, only a few rales at the base of the left lung still remaining.

The white cell count on June 17 (before the commencement of ristocetin therapy) was 9500 per cubic millimetre, falling to 7800 per cubic millimetre on June 20; but on June 23 it was again 9500 per cubic millimetre. His hæmoglobin value was now 10 grammes per 100 ml., and a transfusion of two pints of blood was given to assist his recovery. His chest X-ray film on June 25 showed some clearing in all the areas of haziness.

Prednisolone therapy was continued with diminishing dosage until July 9, novobiocin being given concurrently as a precaution against a flare up of infection. It is interesting to note that culture of his sputum taken on June 26 produced staphylococci and streptococci showing slight sensitivity to chloramphenicol only.

The patient rapidly improved, and by July 5 he was able to walk about and his chest was practically clear on clinical examination. He had a painful ulcerated tongue at this time, but this improved greatly after injections of the vitamin B group. X-ray examinations on July 3 and 23 revealed steady clearing of the lung fields.

On about July 8 he developed very troublesome diarrhœa, which, added to his debilitated condition, was well-nigh fatal. This persisted for six weeks and greatly prolonged his convalescence. The diarrhœa was possibly due to all the antibiotics he had had; but in view of all the different agents he had received, and of the time interval following the use of ristocetin, I do not think that this drug can justly be held responsible.

Comment.

Pneumonia due to staphylococci resistant to antibiotics in general or restricted use is becoming more common in Australia, as it has overseas. Because of the marked propensity for the organism to produce resistant strains to antibiotics the condition will probably become more common, so that the development of other antibacterial agents to meet this contingency continues to be necessary.

The restricted use of the newer antibacterial agents in this country has been very wise, and must be continued, for in desperate cases such as the one here described, the use of an antibiotic to which the staphylococcus has not been previously exposed can be life-saving.

The clinical response to the use of ristocetin ("Spontin") was dramatic, and the antibiotic was undoubtedly life-saving in this instance.

It should be noted that massive doses of penicillin, in the manner described for such cases (Degotardi, 1958), could not be used for this man, because of his allergic reaction to this antibiotic.

Summary.

1. The clinical course of a desperately severe case of staphylococcal pneumonia is described.

2. A dramatic response to ristocetin ("Spontin") was obtained. This drug is as yet available only in limited quantities, but in this case has shown itself to be a valuable weapon to be kept in reserve for staphylococcal infections not responding to other antibiotics. Its present very high cost makes its use unlikely in less severe cases.

Acknowledgements.

I wish to thank Dr. D. Nathan for his help as a consultant in this case, and the sisters and nursing staff of St. Luke's Hospital for their ministrations. I also wish to thank Warland Browne & Son and the Melbourne representative of Abbott Laboratories for making available a supply of "Spontin" at such short notice.

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Addendum.

Since this article was written, the patient improved satisfactorily until he suddenly again became ill on October 10; he was found to have reticulosarcoma, and died on November 9, 1958. There is some evidence that this condition was already present when the foregoing events were recorded; but it is thought that this does not in any way alter the validity of this report.

PSYCHOLOGICAL MANAGEMENT WITH HYPNOSIS FOR A SEVERELY BURNT GIRL.

By JOHN WOODLEY, F.F.A.R.C.S., F.F.A.R.A.C.S., D.A.,
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WE have a patient being treated at the General Hospital, Launceston, for burns of 25% of her body surface, mostly second degree; all were posterior and were below the waist, on the buttocks and on the backs of the thighs and the upper part of the calves. The patient, a girl, aged 16 years, was standing with her back towards an open fire on February 28, 1958; her dress, petticoat and panties caught alight and flared rapidly, being extinguished with the aid of a blanket. She was admitted to hospital four hours later, and in the meantime her sister had smeared butter on the burnt areas. She was otherwise healthy, but mentally dull, her probable mental age being about nine to 10 years. Over the course of the next few weeks, her treatment was along standard lines, with transfusions, sedatives, antibiotics, vitamins, saline baths and excision of eschars. The burnt areas were soon heavily infected with *Staphylococcus aureus* and *Pseudomonas pyocyanea*.

On April 16, seven weeks after the accident, I asked permission of Mr. Alan B. Holmes, the surgeon in charge, to attempt to reduce the patient's pain and boost her appetite with suggestive therapy under hypnosis, having been stimulated by reading an article by Crasilneck *et alii* (1955). At that time the patient was very ill, both physically and mentally. She was incontinent of urine and fæces, had no appetite, was wasted to a mere skeleton, was very drowsy; there were large, deep pressure ulcers reaching to the underlying bone over the knee caps and the anterior superior iliac spines. Even her chin and breasts were showing signs of becoming ulcerated, because she was obliged to lie in the prone position. This made nursing difficult, the patient being unable to help herself. She had to be fed. Every two hours she was lifted, so that a kidney dish could be slipped under her for toilet purposes in an attempt to keep her bed dry and clean. She was extremely odorous, and was isolated in a small room which was, by force of circumstances, in a very dark and gloomy part of the hospital. She needed 1·5 grains of pentobarbitone each night, and had been having half a grain of phenobarbitone three times a day for a month. The giving of saline baths was a very painful process, her pain tolerance being greatly diminished as a result of her recent experiences and lowered morale.

Many badly burnt patients become very depressed and morose, querulous and non-cooperative. This condition increases rapidly during the weeks immediately following the injury, and is aggravated by pain, fast-developing anæmia and toxæmia from secondary infection. Anorexia and starvation ensue, and a vicious circle is created. Drug sedation, which is so necessary, increases the anorexia. Every nursing procedure, however minor, is dreaded. In spite of treatment, this girl's hæmoglobin value fell from 15 grammes per 100 ml. on her admission to hospital down to 6·6 grammes per 100 ml. five weeks after the accident.

Psychotherapy in these cases is essential.

Although of low intelligence, the patient proved a fair subject for hypnosis. Incidentally, the word "hypnosis" has never been mentioned before her. I started by suggesting progressive relaxation and comfort of the limbs, trunk and head, accompanied by a feeling of increasing sleepiness, at the same time gently stroking the back of her neck to help focus her attention. After about 15 minutes, suggestions of "good appetite" and "a feeling of hunger developing", and "getting better daily" were given. The session ended with the patient's being told to wake up feeling well and happy, during counting up to five. The next day this procedure was repeated, but it was decided to test the degree of hypnosis and intensify it by suggesting that the clasped hands were stuck together and could not be separated without permission; this was successful, so that the eyelids and lips in turn were stuck together, and the tongue was made stiff so that speech was not possible. Then analgesia of the forearm was produced, and sterile needles were run through with no reaction of pain or awareness.

On the third day this was repeated, and suggestions of hunger, healing, and sleeping well at night were given; all sedatives, phenobarbitone and pentobarbitone, were stopped, and it was suggested that the patient was able to feed herself. She was then presented with a good lunch, which she attacked voraciously, and she has been eating well ever since. Also, she has never at any time since needed sedatives. During this session it was suggested that the two-hourly lifting of the patient for the kidney dish, and the daily saline baths, would be painless, comfortable procedures; this has been so from that day.

On the fifth day the patient was transferred to a sunny ward on the other side of the corridor. No long-term patient should be in dark, depressing surroundings, but everything should be done to boost morale.

April 23, 1958, was the day chosen for the first skin graft. Prior to this, surgery had consisted of cleaning the burnt areas and excision of eschars. Before the patient went to the operating theatre, it was suggested under hypnosis that the whole back and any part to be touched by the surgeon would be numb and wooden, and that no pain would be felt. However, the patient, when awake, requested an anæsthetic as well, so that nitrous oxide and oxygen (70% and 30%) were given, after one third of a grain of "Omnopon" and one one-hundred-and-fiftieth of a grain of scopolamine had been exhibited one and a half hours previously. No other drug was used, and the patient was fully cooperative; all the skin from the donor areas was shaved off under this combination of hypnotic suggestion and nitrous oxide analgesia, with no reaction from the patient apart from slight movement of the arms and head. She was awake and smiling immediately the face mask was withdrawn. Until now the patient had received daily hypnotic sessions four or five times in each week, in which the suggestions of healing, eating well and sleeping well were always repeated.

On May 2 the patient was still occasionally incontinent of urine and fæces, and she had formed the bad habit of allowing her hands to wander, so that she soiled her hands and pillow with fæces. The nursing staff had had to isolate her eating utensils. This habit was readily eliminated by suggestion, and there was no further trouble. It was also possible to arrange painless venepuncture for blood tests, and to convert temporary fits of depression to feelings of happiness in five-minute sessions. Three weeks after the commencement of hypnotherapy, the *rapport* between patient and therapist was at its peak. To occupy her more fully, it was arranged that the Red Cross workers supply handicrafts, and whenever possible a second patient occupied the other bed in the ward. The patient, in her craving for companionship, had actually named the empty bed "Gladys".

The patient had by then tried occasional walking along the corridor, supported by a physiotherapist and a nurse. Under the influence of post-hypnotic suggestion she walked frequently and increasingly well, at first with a walking frame without assistance from a nurse, and after a day or two with no support at all. It was found that her knee flexion could be improved so that both knees flexed to 90° and better, whereas at that time the physiotherapist could achieve only perhaps 60°.

On May 15 the patient visited the operating theatre for further skin grafts. Again, a combination of hypnosis and

nitrous oxide was used, and the success was just as before; the patient was alert and smiling immediately the face mask was removed.

Five weeks after the commencement of this form of physiotherapy there was an outstanding improvement in all the burnt areas, the pressure ulcers were almost healed and the patient had gained considerably in weight. After the first two weeks of this treatment the sessions had been reduced to three a week, and after four weeks, to one a week, so that the patient would not become too dependent on the therapist.

In the sixth week it was arranged that the patient attend the hospital cinema. She went on a trolly, lying on her face, covered with a cradle and sterile sheet, with blocks to elevate the head end and to reduce the strain from watching the screen. This proved a great success, and kept the patient well occupied with anticipation and realization for at least two days a week. She has paid regular visits to the cinema each week since, and would not want to miss it.

After nine weeks we had the pleasure of seeing the pressure sores completely healed and 95% of the burnt areas healed. It was possible to present her at the Tasmanian State Meeting of the Royal Australasian College of Surgeons.

Until then—June 21—the patient had never been able to sit down since her accident nearly four months previously, so that it was decided to try sitting. This was accomplished with great stiffness and fear, so that the patient was hypnotized and given the appropriate suggestions; she found that she could sit, relaxed and without discomfort, on a pillow placed on the seat of an ordinary chair, with another pillow behind her. This formed a definite milestone in the patient's progress; the fact that she could sit down represented a return to normality enhanced by certain logical consequences—for example, the patient could now sit down to eat her meals, whereas until then she had taken them while standing, and before that she had taken them while lying face downwards, and initially she had actually been fed by the nurses while in this position. The psychological boost to her morale must have been great. Another physical achievement which meant much to the girl was the ability to walk up and down stairs, this rehabilitation being started at that time under the guidance of the physiotherapist. Stiffness in the hip joints increased the difficulty of sitting and climbing stairs, and it was found possible to increase the flexion considerably under hypnosis; but this flexion put such a stretch on the newly-healed lumbar and sacral regions that it was decided to leave this exercise to the more gradual improvement being obtained by the physiotherapist.

On July 2 further skin grafting was carried out on the very small remaining raw areas. Once more a mixture of hypnosis and nitrous oxide was used successfully, but the nitrous oxide was turned off, the patient being left breathing oxygen only, after the first graft was cut. Further grafts were cut, no more nitrous oxide being used; this proved that the addition of nitrous oxide was really unnecessary. As usual, the patient was awake and smiling when the mask was removed.

Now her treatment is virtually completed, and a statement on the time factor may be of interest. The time spent with the patient was an aggregate of two and a half hours per week during the first two weeks, one and a half hours per week during the third and fourth weeks, and thereafter half an hour per week, with occasional periods of five minutes at a time. A full-time medical officer in a hospital could probably manage it better than a member of the honorary visiting staff, as the times can then be arranged to fit in with normal duties. A single-bed quiet ward is necessary, unless a two-bed ward is used, in which case it must be possible to move out the other patient during treatment sessions.

Acknowledgement.

I should like to thank Mr. Alan B. Holmes, the surgeon in charge of the patient, for his complete cooperation.

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Reviews.

Medicine: Essentials for Practitioners and Students. By G. E. Beaumont, M.A., D.M., F.R.C.P., D.P.H.; Seventh Edition; 1958. London: J. and A. Churchill, Limited. 9" × 5½", pp. 868, with 67 illustrations. Price: 45s. (English).

THE previous edition of this book appeared in 1953, and it has consequently needed extensive revision. New articles have been written on a great many subjects, and a completely new chapter is included on the subject of water and electrolytic balance. In addition much of the book has been heavily revised or rewritten. The author's aim from the first has been to produce a text-book of medicine which is not too long for the use of the student preparing for his final examination, and which will also be of assistance to the general practitioner. It is gratifying therefore that he has kept the length of the book almost constant, and has yet coped with the rapid advances in medicine, at least to the extent demanded by his book and its purpose. It should continue to be acceptable to those for whom it is written.

A Doctor in Korea: The Story of Charles McLaren, M.D. By Esmond W. New; foreword by the Reverend George Anderson; 1958. Sydney: The Australian Presbyterian Board of Missions. 8½" × 5½", pp. 58, with many illustrations. Price: 10s. 6d.

CHARLES INGLIS MCLAREN died in Melbourne on October 9, 1957, after an eventful life, much of which had been spent in Korea as a missionary of the Presbyterian Church. This account of his life by one of his friends is not a formal obituary but a simple and sensitive appreciation of the man. Born in Japan of missionary parents, Charles McLaren spent his school and university days in Melbourne. Five years after graduation and within a few weeks of marriage he became a medical missionary in Korea. From then on his life was rich and eventful, involving as it did the Japanese occupation of Korea and two world wars in which he was closely involved; and even after his return to Australia in 1942, right up to the time of his death, he lived a full and active life. He possessed energy, intelligence, character and faith in generous measure. His biographer has portrayed him with sincerity and skill.

Biochemistry and the Central Nervous System. By Henry McIlwain, Ph.D., D.Sc.; Second Edition; 1958. London: J. and A. Churchill, Limited. 9¼" × 5½", pp. 296, with 34 tables. Price: 45s. (English).

THE first edition of this book appeared in 1955. A second edition has just appeared. The changes and additions in the new edition show how rapidly biochemical studies on the central nervous system are developing. More than one quarter of the book has been newly written, and in the rest are numerous alterations. Where it has been thought that useful information could be obtained from subjects such as pharmacology and endocrinology, which would help in an understanding of the biochemistry of the nervous system, this has been freely used. The methods used for the study of general cellular biochemistry have been used to great advantage in the study of nervous tissues. The general metabolism of the brain *in situ* in health and disease is treated at some length. Results of investigations on the enzyme system in brain slices, mashed brain and cell-free extracts of brain tissue are presented very clearly. There is a large section on the composition of the brain and factors which affect this. A section is given to the chemical and enzymatic make-up of the brain during development, and there is a great deal of discussion on chemical factors in nervous transmission. An interesting section is on the effects of depressants and excitants on the central nervous sytem. The whole book is a very complete account of present knowledge on the biochemistry of the central nervous system, written by a man who has probably done more than anybody to advance this knowledge. The book is well written, easy to read and for the most part, not too difficult for the reader whose knowledge of modern biochemistry is not very great. Anyone wishing to study the central nervous system will find much profit in reading this book.

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ON ANEURYSMS.

ONE of the most exciting facets of modern surgical development is the aggressive and largely successful attack which has been made on arterial aneurysms. The pioneering efforts of men such as Anel in 1710 and John Hunter in 1785, who attempted to deal with these lesions by ligation, were courageous but frequently unavailing. From this distance in time, one can only wonder at the magnificent daring of Astley Cooper, who in 1808, without anæsthesia or antisepsis, tied a ligature transperitoneally around the aorta of a patient, aged thirty-six years, who had suffered repeated hæmorrhages from an aneurysm of the iliac artery. Rudolph Matas, of New Orleans, added greatly to our knowledge of these lesions, and by the operation of endo-aneurysmorrhaphy, which he described in 1888, provided at least one reasonably effective method of dealing with them. Then began an era in which ingenuity and skill were constantly pitted against a difficult and hazardous condition. The failures were many, the successes few, but the compulsion remained—the greatest compulsion of all—success meant life, and failure spelled death. Over the past decade immense progress has been made in this field, and the resection of aneurysms with restoration of the continuity of the circulation has emerged triumphantly from the turmoil and has now become an established procedure. It is no longer a matter of principle but simply one of detail, and the respective merits of homograft and prosthesis are being evaluated rapidly.

Of all aneurysms, perhaps the most dramatic and arresting are those which affect the abdominal aorta. Sometimes the lesion may be quite silent, but more often an increasing pulsatile swelling is apparent in the abdomen, and when it erodes the lumbar vertebræ severe pain of a continuous nature is experienced. The natural history of these aneurysms is one of enlargement and, if they are untreated, of ultimate rupture. Nine out of ten of them occur below the renal arteries, and many involve the bifurcation and one or both common iliac arteries. They are almost exclusively, in this country at any rate, atherosclerotic in origin and are, therefore, found in the older age group; but they have been seen in patients as young as the mid-forties, and are frequently found in otherwise fit individuals in their fifth and sixth decades. The only branch of importance which emerges from the infrarenal part of the aorta is the inferior mesenteric artery; this vessel is frequently thrombosed by extension into it of the clot which develops in the convexity of the aneurysm. A collateral circulation to the left side of the colon is usually established quite early, so that resection of the aneurysm with its replacement by a prefabricated prosthesis is an eminently successful procedure. Both from Australia and from abroad reports of successful series of operations of this nature are continually coming to hand, the success rate being much greater when operation is undertaken before the aneurysm has ruptured.

Once major leakage has occurred, the picture changes, and the results of surgery are not nearly so happy. If the leakage is comparatively small, and treatment can be instituted quickly, a good result can be expected; but once repeated hæmorrhages have occurred, and shock of a profound nature has developed, then the operation becomes progressively more hazardous and the results consequently become less successful. In this issue Professor John Loewenthal and members of his group (see page 137) have outlined in some detail the clinical picture which appears with leakage from an abdominal aortic aneurysm. From this report it is clear that a characteristic symptom-complex develops which requires appraisal and recognition if lives are not to be needlessly lost. A clinical triad is regularly observed—pain, shock and abdominal swelling. The pain is intense and may vary in its site with successive leakages. The shock is profound and is not entirely accounted for by the amount of blood loss, but it is probably—at least partly—the result of disruption of the great autonomic centres in the retroperitoneal tissues and in the splanchnic bed. The abdominal mass may be a tender pulsatile swelling, which is quite diagnostic, or it may be a non-pulsatile but tender tumour, the result of extravasated blood. Patients with a vascular tree which is sufficiently degenerated to allow the development of lesions such as these cannot stand repeated episodes of gross bleeding and hypotension and then be expected to survive a prolonged and difficult operation—an operation which is made many times more hazardous by the presence of masses of blood clot spread throughout the loose retroperitoneal connective tissue planes. For those who do survive operation, major difficulties still remain to be overcome. Of these, perhaps the main ones are those affecting the kidney, as the periods of shock and hypotension may have induced a lower nephron nephrosis, and the rapid absorption of large quantities of potassium from the extravasated blood may overwhelm the patient, even though temporarily successful attempts are made to reduce the hyperpotassæmia by dialysis with the artificial kidney. Therefore, it can readily be appreciated that the longer the period after the initial rupture, the greater are the number of incidents of hæmorrhage and shock, and the less likely are the chances of success from surgery. Unquestionably the time to deal with these lesions is before any rupture has taken place, and in skilled hands the results are already thoroughly satisfactory. With increasing experience, even further improvement can reasonably be expected. But once rupture has occurred, the problem becomes greatly complicated.

How can the prognosis of the patient with a leaking abdominal aneurysm be improved? The first necessity is for a wider appreciation and a clearer recognition

of the clinical picture, which so characteristically presents. If the clinical triad is appreciated in its full significance, the many other alternative diagnoses that have been postulated in the past will be avoided, and the condition will be evaluated more accurately. The second necessity is for it to be treated by the fully organized team. This is no complaint to be handled by the individual surgeon. The skilled anæsthetist is of basic importance, and he must be in charge of the extensive resuscitation measures which may be required before, during and after operation. Special instruments are needed for controlling the great vessels involved, and a supply of the appropriate prostheses must be to hand. The assistance of the biochemist and the hæmatologist is regularly required, and adequate supplies of properly matched blood must be ready. Then, and only then, can the surgeon trained in the techniques of arterial anastomosis expect to obtain satisfactory results.

It is, therefore, clearly a problem for the large institution and for the well trained surgical team. While it is true that once hæmorrhage has occurred from an aortic aneurysm the patient is at mortal risk, it is also true that the succeeding hæmorrhages may not occur for days or even weeks subsequently; so that if the condition is recognized with the first episode of bleeding, it is possible to transport the patient to a suitable centre and to institute appropriate measures immediately on his arrival there. The gravest danger lies in a lack of appreciation of the true significance of the clinical state, and thereby the opportunity for one of the truly great efforts of modern surgical salvage becomes irretrievably lost. This type of opportunity may knock once or twice, but rarely more often.

Current Comment.

A NEW USE FOR THE RESPIRATORY PASSAGES.

IT is generally accepted that the *raison d'être* of the respiratory tract is the intake of adequate air. There are, of course, occasions on which other substances are inhaled for therapeutic purposes—a perfectly normal procedure, whose origins are buried in the fields of antiquity. Now and again a foreign body is inhaled by accident, and this untoward event is well known in medical practice. However, a story comes from France which provides an example of a highly specialized use for the respiratory passages. R. Edwards[1] recounts the history of one Mr. P., a shoemaker, who appeared first in December, 1957, with the complaint that he had accidentally inhaled two nails. He was a man of 50 years, who appeared perfectly normal. A radiological examination revealed a nail in the lower lobe of the right lung and another in the lower lobe of the left lung. On inquiry, it was found that he had inhaled the nails three weeks before, and that he had not sought treatment earlier because he feared that the incident might damage his professional status. At bronchoscopy the nails were easily removed, antibiotics were given as cover for a few days, tetanus antiserum was administered, and the incident closed without any complications.

In July, 1958, the patient presented himself again, made himself known, and said that he had again inhaled a foreign body—this time a small pebble. Edwards not unnaturally expressed surprise at the ease with which Mr. P. had inhaled it, upon which the latter tremblingly informed him that he had changed his trade, and that he was being pursued by a psychiatrist. Once more the foreign body was removed, once more the patient was "disinfected"; Edwards then made contact with the psychiatrist colleague who had been mentioned, to learn his opinion of the patient. The psychiatrist regretted that there was nothing to be done, in view of the patient's absolutely normal behaviour except in this one thing: when he was seized with the urge to inhale an object, he was in the same state as an alcoholic faced with a glass of wine. Unless the doctor was there at the time to stop him, nothing else could.

One month later, Mr. P. turned up again, having, as he said, inhaled a metal object. When removed, it turned out to be a lead seal, of the type used on parcels sent by post. Three weeks later, the patient paid another visit—but this time no bronchoscopic examination was performed, since he had coughed up the little pebble he had inhaled. He was considerably annoyed at having got rid of it himself, as he had been when the lead seal was removed. On that occasion, he said that he had tried to inhale two, but had been obliged to swallow the second.

Again, early in 1959, Mr. P. made a further entrance on the stage, and at bronchoscopy a button, a pebble and a piece of glass were removed. Somewhat despairingly, Edwards asks: "When will this fishing expedition end?" He requested his psychiatrist friend to make another attempt at persuading the patient to abandon his habit, adding his own entreaties. However, the situation being what it is, he has opened a special box for Mr. P., the contents of which are increasing in number and interest.

It seems that Mr. P. must be one of those for whom, in the words of Young, "true happiness ne'er entered at an eye". Further comment on his story is unnecessary.

[1] *Presse méd.*, 1959, 67: 788 (April 18).

CANCER OF THE PROSTATE.

PRIOR to the publication in 1941 of the work of C. V. Huggins and his colleagues, little could be offered to victims of cancer of the prostate except palliative relief of urinary obstruction. Since then, the introduction of œstrogen therapy has revolutionized the immediate outlook for a large proportion of sufferers from this condition; but hormone therapy offers only a reprieve, not a cure, and the majority of these patients still die of the disease. A symposium on carcinoma of the prostate held during the Fourteenth Annual Meeting of the British Association of Urological Surgeons, in June, 1958, produced an interesting series of papers which have now been published, on the problems involved. In an introduction to the discussion Arthur Jacobs[1] begins by pointing out that a considerable percentage of men over 50 years of age harbour a latent carcinoma of the prostate, which in the great majority of cases never becomes active. This has been confirmed by various investigators, and the incidence of carcinoma of the prostate found at autopsy depends not on the criteria of malignancy employed, but on the thoroughness with which the search is made. For this reason, survival rates after radical prostatectomy should be interpreted cautiously, since early (and often asymptomatic) carcinomas are the ones considered as particularly suitable for radical operation, but such lesions may remain dormant if undisturbed. Jacobs states that routine examination aiming at the detection of unsuspected neoplastic lesions of the prostate are not customary in Great Britain, and asks what attitude should be taken towards such examinations. Routine examinations can be expected to lead to a positive histological diagnosis in about one out of every four patients over 50 years of age. According to Jacobs, diligence in the search for prostatic cancer at a stage when it can be removed in its entirety has enabled some urologists to carry out radical surgery on up to 20% of their patients, but that a more general experience is that only about 5% of patients are seen early enough for attempts at surgical cure. He concludes by saying that the main questions requiring discussion are: (i) the methods to be used

[1] *Brit. J. Urol.*, 1958, 30: 381 (December).

in the diagnosis of the early malignant lesion; (ii) the treatment to be employed when a positive diagnosis is made in the preclinical stage; (iii) the optimum form and dosage of hormone therapy; (iv) the role of endocrine surgery; (v) the scope and technique of radical prostatectomy.

L. M. Franks[1] discusses the long-term results of endocrine treatment of prostatic cancer. He states that it is now well known that the inner group of prostatic glands gives rise to benign hyperplasia, while carcinoma almost invariably begins in the outer group. Therefore, in carcinoma, early invasion of the capsule occurs with involvement of the perineural lymphatics and the blood vessels in the periprostatic tissues. Surgical removal, with hope of complete cure, is therefore applicable in only very few cases, and endocrine control of this disease has come to be of great importance. Androgen is the physiological activator of the prostate gland, which will atrophy if castration is performed. However, the endocrine system is normally in a state of balance, and disturbance of one part is followed by compensatory reaction in the other. Thus, after castration there is often an increased production of androgen by the adrenal cortex. In addition, other hormones, particularly the gonadotrophins of the pituitary, affect the prostate, so the problem is not a simple one. Huggins, in 1941, suggested that since many prostatic cancers consisted of well-differentiated cells resembling those of the normal prostate, they should react to anti-androgenic treatment by becoming atrophied; and the response in many cases is dramatic, both clinically and histologically. However, there are reasons for thinking that the original concept of anti-androgenic treatment is not altogether satisfactory. Cases have been reported in which clinical improvement occurred after treatment with testosterone, and in another investigation in only six out of 21 cases was treatment with testosterone followed by exacerbation of the growth. Franks considers that these findings underline the fact that we do not know the mechanisms of the response to hormone treatment; in particular, we do not know whether œstrogen acts directly on the tumour cells or indirectly by suppressing pituitary activity, though there is some evidence to suggest that there may be a local effect at first. Franks states that published figures indicate that about 70% to 75% of treated patients and 85% of untreated patients die within three years. This includes an estimated 20% of all cases in which there is no response to endocrine treatment, and the patients die within the first year. After three years the difference in survival between treated and untreated patients becomes more marked; by five years, 25% to 30% of the treated patients are still alive (in other words, most treated patients who survive for three years are still alive after five years). It is presumably among the 5% who would have survived for five years with or without treatment that most of the really long-term survivals occur.

In another paper on endocrine-control therapy in prostatic cancer, J. D. Fergusson[2] reviews the results of treatment in an unselected group of 344 consecutive cases of prostatic carcinoma in which he had been personally responsible. Fifty-six of the patients had not received hormone treatment, and all of these had died within three years or were untraced. All the remainder had been followed up to the time of death or were still alive, and 150 were available for calculation of five-year survival times. In his earlier cases in which the patients were treated by hormones, Fergusson used maintenance doses of 5 to 15 mg. of stilbœstrol daily. While the figures which he produces of the proportion who showed no response to endocrine therapy (18%) and of the proportion (25%) of treated patients surviving at the end of five years, agree closely with those quoted by Franks, his conclusions appear somewhat different. In his series, 73% of untreated patients died within the first six months, but only 34% of those receiving hormone therapy did so. After six months the mortality rates for treated and untreated patients continued almost parallel, but all the untreated patients had died at the end of 36 months, whereas a quarter of the treated cases survived for at least five years. Fergusson concludes that the major importance of œstrogen therapy may lie in the suppression of malignant activity during the first six to twelve months, after which a large number of growths seem to remain controlled or to progress comparatively slowly on sustained treatment. He considers that there is no reliable index of hormone sensitivity, and that the only prognostic data of value are age (the disease tends to take a more chronic course in those over 70 years of age) and the presence or absence of metastases.

Nineteen of Fergusson's patients who had relapsed after œstrogen therapy and castration were subjected to adrenalectomy. The primary indication for operation on all these patients was severe metastatic pain. Six died in the early post-operative period, but eleven of the remainder enjoyed a period of marked symptomatic relief after the operation. However, adrenalectomy was abandoned after the introduction of pituitary irradiation, and since August, 1955, 14 of Fergusson's patients have been treated by this method, involving the introduction of radioactive gold seeds or yttrium rods by the transnasal route, with gratifying results in a number of cases; again, this method is reserved for patients in relapse, since it is regarded as too uncertain for use as a primary definitive treatment. In conclusion, Fergusson advocates initial treatment with high doses of œstrogen in all active cases, supplemented where necessary by castration. He considers that no treatment is indicated for latent cancer.

The remaining three papers in this symposium may be considered briefly. W. H. Graham[3] describes a technique of transrectal prostatic biopsy which he regards as a constructive addition to the available methods of dianosis. J. Bamforth[3] discusses the cytological diagnosis of carcinoma of the prostate. T. Millin[3] contributes a paper on the surgery of the malignant prostate, and concludes that probably not more than 5% of patients with carcinoma of the prostate seen in clinical practice are suitable for radical prostatectomy. The results of œstrogen therapy, combined when necessary with perurethral resection, are sufficiently satisfactory to warrant the use of radical surgery only when a real hope of ultimate cure can be anticipated. The main exception to this is the hormone-independent type of growth with marked symptoms, for which Millin considers surgical intervention justified even if cure is not possible. Finally, in the report of the ensuing discussion, L. Roehl,[4] of Sweden, and C. D. Goodhope, of Washington, refer to "Estradurin", a new water-soluble, long-acting œstrogen. Roehl states that it was given to 85 patients at Lund in a dosage of 80 to 160 mg., administered by intramuscular injection, at intervals of from four to six weeks. Goodhope refers to the results of its use in 110 patients who had been maintained on monthly injections of 40 mg. He states that in 93% improved results were obtained, as compared with the previous œstrogen therapy, including some patients whose tumours appeared to have become hormone-independent when "Estradurin" therapy was instituted. In his view it appears to be the treatment of choice at present in the hormonal management of carcinoma of the prostate.

[1] *Brit. J. Urol.*, 1958, 30: 383 (December).
[2] *Ibidem*: 397.

A RESOURCEFUL DOCTOR.

The indefatigable compiler of our "Out of the Past" column has come up with many interesting items bearing on Australian medicine in past years. We felt, however, that the following advertisement, found in *The Sydney Morning Herald* of March 3, 1897, was such a delectable morsel as to warrant special prominence:

> Will any lady assist an M.D. to establish a practice, with a view to matrimony. Doctor this office.

[1] *Brit. J. Urol.*, 1958, 30: 389 (December).
[2] *Ibidem*: 392.
[3] *Ibidem*: 407.
[4] *Ibidem*: 411.

Abstracts from Medical Literature.

NEUROLOGY AND PSYCHIATRY.

Extraocular Motor Disturbances in Primary Brain Tumours.

T. C. PARSONS (*A.M.A. Arch. Neurol. Psychiat.*, February, 1959) compares his findings in a series of 235 cases with a series of 1132 cases of cerebral tumours collected from the literature. In his series extraocular motor disturbances are encountered in approximately one-quarter of all cases of brain tumours. However, he found oculomotor nerve palsies almost twice as common as abducens nerve palsies in contrast to what had previously been stated in the larger series. The type of extraocular motor involvement is related to the location rather than to the type of tumour. Unilateral involvement of either nerve suggests the presence of a hemispheric lesion; unilateral oculomotor palsy is especially characteristic of temporal lobe lesions. Bilateral or multiple extraocular motor nerve signs suggest basilar or brain stem lesions. The presence of extraocular motor nerve involvement suggests, in his series, increased intracranial pressure in temporal and hemispheric tumours.

Diagnosis of Death of the Central Nervous System.

P. WERTHEIMER *et alii* (*Presse méd.*, January 17, 1959) describe a method of determining the death of the central nervous system when respiration has been maintained artificially for long periods. They state that efficient present-day apparatus has made it possible to keep patients with prolonged respiratory arrest alive for several days or even weeks. It seems that such attempts at resuscitation should be abandoned if the death of the central nervous system can be established beyond doubt. They suggest a study of the electric activity of the brain, the information being obtained not from the scalp but by means of an electrode inserted through a trephine hole into the median thalamic structures. Absence of all cortical and diencephalic activity, verified several times, establishes the death of these centres. Failure of the heart to react to various stimuli establishes the cessation of bulbar activity. When these two sets of conditions are present together, the chance that spontaneous respiration will be restored appears slight, if not non-existent. The question then arises whether artificial respiration should not be abandoned.

Small Tumours Encountered in the Temporal Lobe.

J. B. CAVANAGH (*Brain*, September, 1958) describes in detail the pathological findings in eight patients who underwent unilateral temporal lobectomy because of long-standing and intractable psychomotor epilepsy, often accompanied by disorder of character and behaviour. In six patients symptoms had been present for five years or more and in two the duration was as long as 14 years. Electroencephalographic abnormalities were present in all cases, but the pre-operative air encephalograms showed only minor changes. This small group of eight patients comprised 10% to 12% of a larger series subjected to lobectomy, and was selected because in each instance a tumour-like nodule was found in the deeper part of the temporal lobe on careful sectioning. Only in one case was there any histological evidence of malignancy, and the authors suggest that they may be hamartomatous in nature and that they may be considered as potential points for the further development of gliomas.

Cervical Arthropathy in Syringomyelia, Tabes Dorsalis and Diabetes.

W. A. BRAIN AND M. WILKINSON (*Brain*, September, 1958) made an X-ray examination of the cervical vertebræ of 52 patients with proved syringomyelia. Significant changes were detected in the skiagrams of 24 patients. The incidence was unrelated to the duration of symptoms and there was no direct correlation between the severity of the changes seen on X-ray examination and the extent of the analgesia, although some degree of analgesia was present in all cases, and there did seem to be a greater tendency for such changes to occur in patients with bilateral sensory loss. Syringomyelic patients with X-ray changes showed an age distribution similar to that of 100 patients with cervical spondylosis. The radiological appearances of cervical arthropathy are described, and the authors conclude that in the earlier stages the X-ray changes are identical with those of cervical spondylosis and that the arthropathy was due to the same causes as cervical spondylosis, the syringomyelia merely serving to intensify the process of degeneration. Reference is made to the arthropathy which may occur in some cases of tabes and diabetes. The details of six illustrative cases are given, and the authors emphasize the possibility that some of the patient's symptoms may be due to the associated arthropathy and that the arthropathy may be responsible for exacerbating the disorder which is its cause.

Thyrotoxic Myopathy.

R. HED, L. KIRSTEIN AND C. LUNDMARK (*J. Neurol. Neurosurg., Psychiat.*, November, 1958) report a detailed study of the musculature in 20 cases of thyrotoxicosis. Ten of the patients had severe muscle weakness, and in the majority of this group symptoms had been present for more than three years. Signs of thyrotoxicosis were slight and eye signs were absent in this group. In the ten other less severely affected patients, the duration of symptoms ranged between six months and one year, and eye signs were present in all but one case. In both groups females predominated, which is in contrast with previously reported series of chronic thyrotoxic myopathy. The muscle weakness and wasting were confined to the proximal muscles except in one case, and in six cases the lower limbs were solely affected. In one patient the pharyngeal and both sterno-mastoid muscles were involved, and in a few instances the muscle weakness preceded the signs of overt thyrotoxicosis. All patients responded to treatment within two months. An impaired carbohydrate metabolism of the diabetic type was found in five of the severely affected group. Muscle biopsy gave a normal result in one and revealed varying degrees of atrophy in 17 other patients. Electromyography in the 17 patients examined showed patchy changes of a myopathic type. The authors suggest that the mild muscle weakness often found in cases of thyrotoxicosis may in fact be caused by a true myopathy, and that thyrotoxicosis untreated for a long period may be one of the principal factors in the origin of disabling thyrotoxic myopathy.

Intracranial Tuberculoma.

C. ARSENI (*J. Neurol. Neurosurg. Psychiat.*, November, 1958) reviews the findings in 201 cases of intracranial tuberculoma treated by surgery. The series constitutes 13% of all patients with expanding intracranial conditions operated upon in Bucharest between the years 1935 and 1957. By far the most common site was the cerebellum, which can be explained by the higher incidence of tuberculoma in children, with a preponderance in the posterior fossa. In patients over the age of 20 years, tuberculomas were equally frequent above and below the tentorium. In 32 cases multiple lesions were present. Patients' ages ranged from three months to 68 years. A history of tuberculous infection was obtained in 52% of the patients. The lungs were the most common site of this infection, with an incidence of 43%. In the remaining cases the tuberculoma was apparently primary. In cases in which the tuberculoma was associated with an active lesion elsewhere, the tuberculoma appeared to develop at a late stage, or several months after the start of the chronic disease. The clinical features were dependent upon the site of the lesion, and in 68% of cases of cerebral tuberculoma focal signs were present. In 72% of patients there were symptoms of intracranial hypertension, whilst 85% had epileptic attacks. Intracranial calcification was seen in 5·5% of cases. Since the introduction of streptomycin, the mortality rate has fallen because of the control of post-operative meningitis, and complete recovery followed operation in 88% of the most recent group of 141 cases in which streptomycin cover was given.

Subarachnoid Hæmorrhage.

W. MCKISSOCK, K. PAINE AND L. WALSH (*J. Neurol. Neurosurg. Psychiat.*, November, 1958) review the findings in 455 cases of subarachnoid hæmorrhage and record a statistical analysis of the results of management of 261 patients with ruptured intracranial aneurysms. In 26% of the series the cause of the hæmorrhage remained unexplained, and the authors emphasize the low mortality in this group (14%), compared with an over-all mortality of 46% in those patients with ruptured aneurysms. Angiography was performed in 253 patients with aneurysms. The anatomical distribution is listed, and in 17% of cases the aneurysms were multiple. Patients are classified according to the severity of their condition on admission to hospital and the time delay since the hæmorrhage had occurred. The results are analysed with reference to the different sites of occur-

rence of the aneurysms and the nature of the surgical treatment, when performed. The mortality was higher, with coma producing hæmorrhage, and hypertension was also found to be an adverse factor. The authors fail to demonstrate any statistical difference in mortality between the treated and untreated patients, and suggest that a pre-planned control series is necessary to answer this controversial matter.

Psychological Characteristics of Children of Chronic Invalids.

S. H. ARNAUD (*Psychosom. Med.*, January-February, 1959) wished to investigate certain psychological characteristics of children who have been exposed to the type of family disruption which occurs when a parent is chronically ill and still remains in the home. To do this he assessed the Rorschach findings in 60 children who had a parent suffering from multiple sclerosis, and compared the records with 221 control children in the same age range (seven to 16 years). The children of multiple sclerotics scored higher in the following categories: body concern, hostility, constraint in interpersonal relations, dependency longings, and they showed a higher incidence of a pattern of false maturity. The author concludes that these findings would be also applicable to children of other non-hospitalized patients with chronic disabling diseases, such as arthritis, which involve considerable role alteration and foster tensions within the home.

THERAPEUTICS.

Dihydrone Pectinate, a New Analgesic.

C. FEILEUX AND P. SERIES (*Presse méd.*, April 11, 1959) have made a clinical trial of dihydrone pectinate as an analgesic agent. They used it over a period of four months, both as a post-operative analgesic and for premedication before operation. They state that in their opinion the drug has an analgesic action equal to that of morphine and pethidine. Its action is longer, so that the daily dose is much lower. The secondary effects are minimal. They intend to use the drug more widely, especially for aged patients, in whose treatment it has fewer disadvantages than morphine.

Fixed Combination of Chlorothiazide-Reserpine in Hypertension.

H. E. NUSSBAUM *et alii* (*Amer. J. med. Sci.*, December, 1958) present a report on the use of a fixed combination of chlorothiazide and reserpine in hypertension, based upon a series of 24 patients with essential hypertension and one with chronic glomerulonephritis. The authors used as the criterion for response a reduction in the mean blood pressure of 20 mm. of mercury or more, or a return to normotensive levels, and found that the over-all response rate to combination therapy of chlorothiazide and reserpine was 54%. They conclude that chlorothiazide is an effective diuretic agent, and at least as potent as the organic mercurials. They note that other investigators have demonstrated significant hypotensive effects with chlorothiazide, but their own experience did not confirm this. Normotensive patients do not show any hypotensive response to the drug. However, the authors consider that chlorothiazide is a useful drug when used in combination with other hypotensive agents. They suggest that the apparent potentiating effect sometimes observed when chlorothiazide is administered with another hypotensive agent may be due to a delay in the excretion of the hypotensive agent caused by chlorothiazide. Certainly, chlorothiazide offers many advantages, both as a diuretic agent and as a hypotensive, in patients with congestive heart failure. The authors note that it is well tolerated, effective, and has been singularly free of serious side effects.

Psoriasis.

V. H. WITTEN *et alii* (*J. Amer. med. Ass.*, February 7, 1959) report the treatment of psoriasis vulgaris with iproniazid ("Marsilid"). They note that others have reported beneficial effects from the administration of iproniazid for psoriasis. Sixteen patients with typical chronic psoriasis who had failed to respond to other treatment were given iproniazid. The disease had lasted from one and a half to 43 years. Initially, 150 mg. per day was given orally in divided doses. If no response occurred in one or two weeks, the dose was increased by 50 mg. every few days until there was a satisfactory therapeutic result or undesirable effects were noted. Only three patients improved, temporarily. The authors state that the disagreeable effects of the drug were so frequent that they did not pursue the investigation.

New Drugs for the Treatment of Hypertension.

R. W. WILKINS (*Ann. intern. Med.*, January, 1959) discusses the subject of new drugs for the treatment of hypertension, and presents a review of the merits and side effects of rauwolfia, hydralazine, veratrum, chlorothiazide, the antiserotonins and the ganglionic blocking agents. All the antihypertensive drugs, with the exception of chlorothiazide, appear to be non-specific, in that they cause similar hypotensive responses in normotensive and in hypertensive individuals. Reduction of arterial pressure, even by such non-specific agents, appears to be a beneficial, if not a life-saving procedure, in many hypertensive patients, particularly those with an accelerated phase or a malignant crisis. Additive if not synergistic effects can be produced by combining the antihypertensive drugs or by using them in combination with splanchnicectomy. The author states that a tendency to hypertension seems to exist in most hypertensive patients, since almost uniformly they become hypertensive again when all therapy is stopped. This trait apparently accounts for the mobilization of counteracting mechanisms to the hypertensive effects of drugs, and explains why the blood pressure overshoots when some of the drugs are suddenly stopped. Although several drugs in combination or in larger doses may be necessary to lower a hypertensive patient's blood pressure to satisfactory levels, it is often possible after some months to maintain such lower levels on considerably less medication than was required to obtain them initially. Serotonin may play a role in hypertension, but it is not clear whether the antihypertensive effects of reserpine, B.A.S. or iproniazid are connected with their effects on serotonin, and if so, how they produce this effect. Ganglion-blocking agents are slowly being replaced in the drug treatment of hypertension, except as a last resort in very critical or very resistant cases. For the usual ambulatory hypertensive patient a persistent long-term trial of conservative doses of rauwolfia, veratrum, hydralazine and chlorothiazide, in combination if and as necessary, will be reasonably successful. High blood pressure of serious degree is harmful, and it can and should be moderated in almost every case. After rarer causes of hypertension, such as coarctation of the aorta, renal disease and adrenal tumours with hyperadrenalism or hyperaldosteronism have been ruled out, antihypertensive drug treatment should be given so as to lower the blood pressure gradually, in every patient in whom the family history and the course of the disease indicate that a shortening of life or a period of invalidism is likely without treatment.

The Treatment of Acne with Tolbutamide.

J. L. COHEN AND A. D. COHEN (*Canadian med. Ass. J.*, April 15, 1959) state that after their attention was drawn to the rapid recovery from moderately severe acne of two women receiving tolbutamide, they tried this drug on 23 additional patients with severe acne and other obstinate pustular infections of the skin. In only one patient did the drug have to be discontinued on account of side effects. The results were excellent in eight patients, good in 12, and fair in five. All patients experienced a sharp decrease in new pustular and cystic lesions and diminution both in size and soreness of the lesions. The dose of tolbutamide administered was 0·5 gramme (one tablet) twice daily for those with severe acne and 0·5 gramme once daily in the milder cases.

Addiction to Pyrrolamidol.

G. BOUDIN AND J. BARBIZET (*Presse méd.*, January 17, 1959) have continued their studies on the use of d-methyl-3-diphenyl - 2, 2 - morpholino - 4 - butyryl pyrrolidine (pyrrolamidol) as an analgesic, particularly to discover whether it causes addiction. They state that, after 18 months, the excellent analgesic properties of the drug and the rarity of habituation have been confirmed. Nevertheless, cases of addiction do occur. The clinical characteristics of addiction to this drug vary, as follows: (i) simple desire for the drug; (ii) attacks of distress, agitation, pain and muscle twitching coming on when the effects of a dose are wearing off; (iii) a progressive increase in the dosage producing a state of irritability, insomnia and loss of weight; this may progress to coma or delirium, and requires urgent treatment. In all the cases in the authors' series, the patients had some type of psycho-pathological disorder. Addiction to the drug is rare, and may be avoided if the clinician takes care to prescribe the drug in accordance with the legal provisions, and with due regard to the patient's psychological make-up.

Medical Societies.

PÆDIATRIC SOCIETY OF VICTORIA.

A MEETING of the Pædiatric Society of Victoria was held on August 13, 1958, at the Royal Children's Hospital, Melbourne.

Lingual Thyroid.

MR. P. JONES said that the occasion was the third on which a patient with lingual thyroid had been shown to the Society, the first having been shown by Dr. Dudley Hagger in 1955. The points of clinical importance to be seen were the incisions for lateral pharyngotomy and tracheotomy, a temporary weakness of the depressor anguli oris (which was diminishing) and a lower right abdominal incision, into which portions of the thyroid tissue had been placed. There was also absence of palpable thyroid gland in the neck. The patient, a female, aged nine years, had attended the Royal Children's Hospital in June, 1958, with a letter from her doctor, who had noted stertorous obstructed breathing during anæsthesia and tonsillectomy for dysarthria one month before. At that time a mass at the back of the tongue had been seen. Her mother had noticed a change in voice, huskiness and dysarthria over the preceding two years. The symptoms were progressive, and recently mild dysphagia had appeared. The patient's early history had been non-contributory, and general examination had revealed no abnormality save a large, pink, globular mass on full depression of the tongue, and a curious feeling of emptiness between the sterno-mastoid muscles and the trachea. A diagnosis of lingual thyroid had been made, and confirmed by radioactive iodine uptake, which was entirely confined to the lingual area. An operation had been carried out a month prior to the meeting. Intubation had been performed via the nose, the passage of the tube into the larynx being "blind" and controlled by finger-tip palpation. Full examination of the patient under anæsthesia confirmed that the thyroid mass was situated too far posteriorly to permit removal by the oral route, and that while median, it extended somewhat more to the right side. Accordingly, a right cervical incision had been made over the digastric triangle. The submandibular gland had been excised and the hyoglossus and the lingual artery divided, the lingual thyroid supply having been controlled before the pharynx was opened. A finger in the mouth had directed the mass into the operative field, where its separation from the tongue had been effected. The mass had measured approximately four centimetres in diameter and was roughly spherical. The mucosal covering had been peeled away and the gland substance cut into cubes of three to four millimetres per side. They had been immediately planted in groups of four to six into the substance of the right rectus muscle. Because the mass had been tucked into the angle between the front of the epiglottis and the back of the tongue, its removal had denuded that area of mucous membrane. A tracheotomy had accordingly been performed as a precautionary measure, and the tube had been removed on the fifth day after operation. The post-operative course was otherwise uneventful. The patient's basal metabolic rate was now -24%, and the serum cholesterol content 380 mg. per 100 ml. It was planned to reassess the level of thyroid activity at monthly intervals, and to administer further I^{131} at a later date to estimate the activity of the transplanted thyroid as judged by its uptake.

Mr. Jones went on to say that there were now some 200 cases of that rare condition in the world literature since Godart's first case in 1760. There had been three cases in 800,000 admissions to the Johns Hopkins University Hospital. Montgomery had analysed 144 cases reported prior to 1936, and his findings in summary were as follows. Of the patients, 45% had presented during puberty and adolescence; two-thirds had no thyroid tissue save that in the tongue. Seven out of eight investigated with I^{131} had shown no evidence of cervical thyroid tissue; the characteristic macroscopic and clinical features were the same as those in the case presented. The microscopic picture was one of normal thyroid tissue in more than 50% of cases; in the remainder there was a fœtal adenoma pattern, or some scattered colloid cysts were present. Carcinomatous change had been reported in nine cases, but was open to considerable doubt. There were difficulties in establishing that diagnosis, for a capsule was frequently absent, and thyroid tissue was found scattered amid the muscle fibres of the tongue. Local "recurrence" might well follow incomplete removal due to inaccessibility.

Mr. Jones finally said that the use of lateral pharyngotomy, first described by Lymphius in 1897, had been fully justified in the case under discussion by the completely satisfactory access, minimal bleeding, smooth post-operative healing and cosmetically acceptable scar. The outcome of the transplant was as yet uncertain; but the previous case reported by Dr. Hagger, in which the operation had been performed by Mr. Lawson, had been successful. Mr. Jones finally thanked Mr. Lawson for his advice concerning the technique of planting the thyroid seeds.

MR. R. LAWSON said that it was now nearly three years since he had transplanted the lingual thyroid of the previous patient to whom Mr. Jones had referred. That patient was now euthyroid. Menstruation had commenced, and had been associated with a tender swelling under the abdominal scar.

DR. H. BREIDAHL referred to the case of a woman, aged 25 years, who still had a lingual thyroid. She suffered no discomfort from it and had undergone a normal pregnancy. Attempts to transplant other endocrine glands had been unsuccessful—both homographs and heterografts had been carried out with the pituitary, the adrenal and the parathyroids. As thyrotrophic hormone was now available, it might be of use in stimulating the transplanted thyroid cells in the rectus.

DR. H. WETTENHALL said that he doubted the significance of the basal metabolic rate and the blood cholesterol level. An estimation of the level of protein-bound iodine would be more useful. He doubted the usefulness of thyrotrophic hormone, as in the presence of hypothyroidism its production by the pituitary was automatically increased.

Probable Fibrocystic Disease of the Pancreas.

DR. B. MARKS then presented the history of a man, aged 44 years, a retired shopkeeper, who had complained of cough and sputum for as long as he could remember, and certainly since the age of two and a half years. His sputum had always been purulent, and had recently increased in amount to two ounces per day. Attacks of pneumonia had occurred at the ages of two and a half, seven, 10, 29 and 34 years. Wheeze had been noted as far back as early childhood. It was relieved each morning by a brief period of chest "clearing". His effort tolerance had been impaired for many years, but he was still able to climb three flights of stairs quite briskly. There were days when he was more wheezy than usual, but the dyspnœa did not alter appreciably. A nasal discharge had been noted since childhood, and was always purulent. His nose was usually blocked and his sense of smell was poor. "Colds" were frequent. The patient's mother did not consider him strong as a child, and he was always careful and looked after himself a good deal. He was considered small as a child, and was the shortest in his class, although his sisters were of normal height. His appetite was always very good, and could even be regarded as voracious, especially in adult life. He had passed two motions daily as a child, and had noted the oozing of oil from his anus from the age of 20 years. After his attack of pneumonia, when aged 29 years, he noted the onset of severe diarrhœa, which had continued since. He always had several loose motions daily, usually five to eight in number, which were often fluid. Pain was unusual with defæcation. The patient's vision had been impaired for two years, and that condition had been relieved at intervals by local cortisone injections. He had been married for many years, but his wife had never been pregnant. Their sterility had been investigated, and his wife had been pronounced normal. Testicular biopsy had been carried out on the patient, and he believed the results to have been normal. The patient's father had died at the age of 69 years of malignant disease. His mother was alive and well, but described as rather wheezy. Two sisters were well. One brother had been stillborn, and the other had died at the age of six months after having had neck retraction for a long period.

Dr. Marks went on to detail the examination findings. He said that the patient was short, slight and wheezy. Bilateral submandibular gland enlargement was present. There was no clubbing of digits. The ântero-posterior diameter of the chest was increased, movement was poor and the area of cardiac dullness was increased. The percussion note was generally hyperresonant, but air entry was quite good. Many rhonchi were audible, and fine crepitations were audible posteriorly up to the angles of the scapulæ. On examination of the fundi, bilateral choroiditis with vitreous opacities was noted. The liver and spleen were impalpable, and general examination revealed no abnormality.

Dr. Marks then showed slides illustrating the investigations performed. An X-ray film of the chest revealed fine pulmonary fibrosis, most marked at the lung bases and in the mid-zones. Bilateral bronchography showed widespread bronchial change of "bronchitic" type, with localized areas of bronchial dilatation in addition. The stools contained many globules of oil, and the presence of gross steatorrhœa was confirmed chemically. Duodenal intubation showed virtual pancreatic achylia, even after an intravenous injection of secretin. Two sweat tests were carried out, and the results were just within the upper limits of normal for an adult. The results of liver function tests were essentially normal. The result of the glucose tolerance test was of the "lag storage" type. An X-ray examination of the abdomen showed no pancreatic calcification. Attempted culture of the sputum yielded no pathogens. Investigation of the patient's seminal fluid was proceeding.

Dr. Marks concluded by mentioning that there had been considerable relief of the patient's cough, sputum production and nasal discharge since the long-term administration of tetracycline. Early results with pancreatic extract given by mouth promised some control of diarrhœa. Dr. Marks expressed his gratitude to Dr. Howard Williams for advice and for carrying out the various investigations, and to Mr. John Hayward who was responsible for the patient's being referred.

DR. CHARLOTTE ANDERSON, in opening the discussion, said that she was grateful to Dr. Marks for referring the patient to the clinical research unit for investigation. She agreed that the diagnosis was most likely to be that of fibrocystic disease of the pancreas, although as far as she knew he was the only patient of that age in whom that condition had been recognized. All features of the history, examination and investigation were in agreement, with the probable exception of the sweat test, but that needed a little comment. Dr. Anderson then referred to the experience of her group with the "sweat test"—the estimation of sodium and chloride content of sweat collected from a patch on the arm. Sweating in that area was stimulated by the intradermal injection of a small dose of mecholyl. During recent years, it had been demonstrated by American workers that the sweat sodium and chloride contents were greatly elevated, and the majority of patients showed levels of over 70 mEq./l. The sweat test had now become the easiest and most reliable confirmatory test in that disease. At the Royal Children's Hospital they had applied the sweat test to 78 patients with fibrocystic disease in the past two years, and had found elevated levels of sodium and chloride in all but five children. One hundred and sixty-two children with no disease showed levels all below 70 mEq./l. except in one case, in which the level was 70 mEq./l. Therefore the upper limit of normal was taken at 70 mEq./l., whilst the usual fibrocystic figures were about 100 to 110 mEq./l. On those figures, that man, with levels of 70 to 85 mEq./l., came into the lower fibrocystic range. However, when a series of parents and normal adults were tested, among 42 mothers and fathers of children with the disease, eight showed sweat chloride levels between 70 and 85 mEq./l. Dr. Anderson said that a patient with the disease did not constantly show all the features. For instance, in large American series, 2% to 3% of patients with other stigmata still had normal sweat electrolyte contents, and 10% of patients did not have complete pancreatic achylia and, in fact, secreted enough enzymes to make fat absorption normal. The degree of chest infection also varied greatly; at times its absence in the early years of life enabled patients to remain unrecognized until later childhood. In a series of 26 normal adults, six showed levels over 70 mEq./l. Therefore, the result in the case under discussion could not be definitely accepted as abnormal in an adult.

Dr. Anderson went on to say that some aspects of the patient's story and investigations led one to suspect that the condition was not complete: first, because he had reached the age of 44 years without incapacitating lung damage, and with fair nutrition; secondly, because his early bowel history suggested that the pancreatic lesion might have been incomplete at that stage, but progressive, as had also been reported in other cases; thirdly, the result of the sweat test was at the doubtful level. Nevertheless, she thought that the diagnosis was most likely, and it was hard to find an alternative one to include all the findings. Regarding the patient's sterility, Dr. Anderson said that she did not know of any other reports of that association, but as far as she could ascertain overseas, although many of the known patients were now entering their early twenties, no marriage had occurred. Bodian had reported pathological changes in the mucous cells of the glands of Littré and Cowper and in the cervix of the uterus.

The family history of the patient under discussion showed some points of interest. He had had a brother, who had died at the age of six months, but that baby had apparently not had a cough—he rather showed neck retraction and retarded development. However, the patient's sister had a family of which three children had died, two in the Royal Children's Hospital. The first had died at ten months with pneumonia in 1917, but no records were available. The second girl had died at the age of 13 years in 1938, under anæsthesia for a bronchogram; she had had cough and sputum most of her life, and was very small and thin. The third child had died of summer diarrhœa and dehydration in Mildura. It was therefore very suggestive that the disease existed in that family.

Dr. Anderson said that she thought the patient under discussion was very worthy of presentation to the Society, because it was of great interest to demonstrate a case in which that condition was first recognized at the age of 44 years, especially to physicians dealing with adults, who might be stimulated to regard with suspicion their adult patients with bronchiectasis and emphysema. She also pointed out that it was not an uncommon condition, being one which affected at least one in every 1000 children born alive, and that now a number of those children were living well into their late teens at least and showed every prospect of surviving further. They would therefore probably come under the care of some of the physicians dealing with adults. Investigation of the figures at the Royal Children's Hospital showed that 108 cases had been encountered in the past five years. Of those patients, 59 had died, mostly under the age of 12 months, with chest infection. However, of the others, many were living fairly normal lives. Dr. Anderson illustrated that fact with reference to 35 patients followed by herself, among whom three were now aged over 14 years, and 18 between eight and 14 years. Eighteen of those 35 children had had no persistent purulent chest infection and needed only occasional antibiotic therapy; 13 had some degree of purulent lung infection which was controlled by continuous therapy, whilst four had severe lung damage. Those figures also indicated that in a considerable number of those children the disease had not been diagnosed till they were over the age of five years, and some had not shown serious chest infection even yet.

Dr. Anderson said that fibrocystic disease of the pancreas was an intriguing disease, in which the disorders of viscid mucus and abnormal sweat were hard to link together, but that the pathological picture which followed as a result of those abnormalities was fairly well understood. Some features of the chest pattern of illness which might put the adult physician on his guard were the diffuse nature of the lesion, the presence of emphysema, and the sticky sputum, with the almost universal presence of *Staphylococcus aureus* often as the only organism in the sputum. It was rather rare in other types of bronchiectasis to find the *Staphylococcus* present at all consistently. She congratulated Dr. Marks on finding the patient, and said that many workers had suspected that adults with the disease might still be alive, but there were no reliable reports of cases being recognized for the first time beyond about the age of 18 years.

DR. E. MACKAY said that both the patient and his wife were now aged 45 years. They had been married in 1929, and a seminal analysis performed in 1937 had revealed no spermatozoa. However, a testicular biopsy had shown some spermatozoa in the testis. The vas deferens had been explored on one side, and the surgeon had expressed the opinion that the patient was permanently sterile.

DR. I. WOOD asked whether submaxillary gland biopsy would help to clinich the diagnosis.

DR. J. PERRY said that he had previously found fatty livers at autopsy in about half the patients dead of fibrocystic disease. The present patient apparently had no liver lesion. Dr. Perry was interested also in the absence of secondary dietetic phenomena.

Metabolic Studies in a Case of Rickets Resistant to Vitamin D.

DR. J. MCCOY said that rickets resistant to vitamin D had been first described in 1937 by Albright, Butler and Bloomberg, who reported the case of a girl, aged 12 years, successfully treated with massive doses of vitamin D. They postulated that the primary defect in vitamin D metabolism affected the intestinal absorption of bone minerals, and that secondary hyperparathyroidism was present as a compensatory mechanism and accounted for the low serum phosphorus level which was typical of the

condition. An alternative theory had been put forward by Robertson, Harris and McCune in the United States, and by Dent in England. Those workers held that the primary defect was diminished renal tubular reabsorption of phosphate which led to hypophosphatæmia; that reduced the solubility product of calcium phosphate, and thus produced rickets. In Europe, Fanconi had supported that concept and coined the name "phosphate diabetes". Dr. McCoy said that a series of cases had been studied with a view to investigating both those theories, and the results in the first case studied were the subject of his paper. Intestinal absorption of calcium was studied by standard balance techniques, and renal tubular transport of phosphate was investigated by estimating the maximal renal tubular reabsorption of phosphate (Tm P) according to the method of Anderson.

The case history was that of a boy, aged 11 years, of Greek Cypriot extraction, who had migrated with his parents to Australia at the age of five years. He had been first examined at the age of eight years and nine months, when Mr. Eric Price had referred him to the clinical research department of the Royal Children's Hospital with the diagnosis of refractory rickets for investigation. The obstetric and neonatal histories were normal. At the age of five months, his left leg was said to have been paralysed, but after six weeks in a plaster cast he could move it normally. He sat up at eight months and stood at 14 months. He attempted to walk at 18 months, but had difficulty, and preferred to hop along rather than walk. At the age of two years his legs were noticed to be bowed. Since that time walking had always been difficult, and he was smaller than his peers. He had been breast fed for the first nine months, and since that time had had a normal diet with supplemental vitamin D and vitamin C in small doses. There were no symptoms referable to the alimentary or renal systems. There was no family history of rickets or of other relevant conditions. On examination of the patient, he was a dwarfed lad with a noticeable limp. He had prominent eyes and a prominent forehead. The head circumference was 53 cm. The feet and hands were broad and stubby. The costo-chondral junctions were beaded, both legs were bowed and he had a lordotic stance. His weight was 22·5 kg., and his height was 114 cm. (upper segment 66 cm., lower segment 48 cm.); his span was 122 cm. His blood pressure was 120/60 mm. of mercury. The opti fundi were normal; no crystals were seen in the corneæ. The remainder of the physical findings were normal. A blood count showed a hæmoglobin value of 9% and a leucocyte count of 9300 per cubic millimetre (40% neutrophils, 59% lymphocytes, 1% eosinophils). No protein or sugar was found in the urine on chemical testing; the urine was microscopically normal (five examinations); paper chromatography showed normal aminoacids and absence of sugars. The plasma electrolyte contents were sodium, 128·0, 144, 140 mEq./l.; potassium, 4·0, 3·4, 3·3 mEq./l.; carbon dioxide, 26·9, 21·9, 23·3 mEq./l.; chloride, 104·0, 105, 103 mEq./l.; calcium, 11·0, 11·0, 12·0 mg. per 100 ml.; phosphate, 2·6, 2·1, 1·9 mg. per 100 ml.; protein, 6·8, 7·1, 6·9 grammes per 100 ml. The hæmatocrit figures were 45%, 45%, 46%. The blood urea content was 24 mg. per 100 ml. The blood pH was 7·45. The serum alkaline phosphatase content was 66 K.-A. units per 100 ml. The results of renal function tests were: (i) water deprivation test (18 hours)—the specific gravity of the urine was 1·027; (ii) creatinine tolerance test—68% fall in the blood level of creatinine in four hours. A fat balance study (daily intake 50 gm.) showed a five-day mean absorption of 94%. Skeletal X-ray films revealed widespread rhachitic changes involving all the long bones and the vertebral column. Dr. McCoy said that those investigations excluded other causes of resistant rickets, and it was considered that the diagnosis was vitamin D resistant rickets. Calcium balance studies and renal function tests were carried out before therapy was commenced. The results of a calcium balance study were: daily intake 938 mg. (100%); fæcal excretion, 917 mg. (98%); urinary excretion, 34 mg. (3%); absorption, 21 mg. (2%); retention, 13 mg. (–1%). Renal function tests gave the following results: glomerular filtration rate, 138 ml. per minute per 1·73 sq. m.; Tm P, 2·1 mg. per minute per 1·73 sq. m.; that gave a glomerular filtration of 1·5 mg. per minute per 100 ml.

Dr. McCoy went on to say that treatment was begun with calciferol (vitamin D_3), in an initial dosage of 150,000 units per day by mouth. That dose was later increased to 500,000 units per day, and was subsequently varied according to serial plasma calcium, phosphate and alkaline phosphatase estimations. The present maintenance dosage was 100,000 units per day. The rhachitic lesions had healed radiologically after four months of treatment.

Prior to bilateral osteotomies to both legs below the knee after two years of treatment, therapy ceased and was not recommenced till immobilization terminated; by that time there had been a fall in the plasma calcium level which, however, was still in the normal range. After twenty-nine months' treatment, the boy weighed 27·3 kg. and his height was 127 cm. Throughout the follow-up study period, the rickets remained healed. Calcium balance and renal studies were repeated, four months and 15 months respectively after the commencement of vitamin D therapy. A calcium balance study gave the following results: daily intake, 976 mg. (100%); fæcal excretion, 378 mg. (39%); urinary excretion, 73 mg. (7%); absorption, 608 mg. (61%); retention, 525 mg. (54%). Estimation of the glomerular filtration rate gave the following figures: 133 ml. per minute per 1·73 sq. m.; Tm P, 2·1 mg. per minute per 1·73 sq. m.; glomerular filtration, 1·5 mg. per minute per 100 ml.

Dr. McCoy said that as a result of therapy there had been a striking change in the intestinal absorption of calcium, which rose to 61% of the intake; having been 2% of the intake before treatment. Four months after commencement of therapy, 89% of that absorbed calcium was being retained in the body, at a time when there was radiological healing of the rickets. That indicated that a marked skeletal deficit of calcium was still present. Renal studies showed a normal glomerular filtration rate and a low Tm P before treatment, and there was no significant change after 15 months of therapy. That was reflected in persistent hypophosphatæmia. It had been necessary to maintain a mild degree of hypercalcæmia in order to prevent relapse of the rickets. The patient withstood that hypercalcæmia without evidence of thirst, polyuria or other symptoms of hypervitaminosis D. Therapy had been temporarily stopped during a period of immobilization following corrective orthopædic surgery, and for a period of two months he maintained his previous plasma calcium level and normal alkaline phosphatase level and the rickets remained healed. When therapy was recommenced, the serum calcium level had fallen to 10·8 mg. per 100 ml., having been 13·5 mg. per 100 ml. when therapy was stopped. After two and a half years' therapy his height and weight were still below the five percentile levels for his age; however, the increase in height of 13 cm. during that period was at the 50 percentile level. Maintenance therapy had to be continued throughout childhood, and probably in most cases in adolescence and adult life, in order to prevent relapse.

Discussing the metabolic studies, Dr. McCoy said that there had clearly been a gross defect in intestinal absorption of calcium, which was corrected by massive therapy with calciferol. Those findings supported the Albright theory; however, studies of renal clearance phosphate had shown defective tubular reabsorption of phosphate before treatment, and that remained unchanged after the rickets had healed. Those latter findings supported the renal tubular theory, as improved intestinal absorption of calcium should have removed the stimulus to secondary hyperparathyroidism and thus allowed an increased maximal renal tubular reabsorption of phosphate. The finding of a persistently low Tm P was corroborated by the persistence of hypophosphatæmia. Dr. McCoy said that those studies therefore showed that both theories of pathogenesis were partly correct in the case discussed.

Discussing the diagnosis of vitamin D resistant rickets, Dr. McCoy said that that depended on the exclusion of other causes of rickets, and finally on a satisfactory response to massive therapy with vitamin D. There were more than 20 causes of rickets, which could result from liver or alimentary disease, from renal disease, from certain inherited metabolic disorders and from metallic poisoning; but a small battery of investigations could usually elucidate a diagnosis of primary vitamin D resistant rickets. Such investigations included measurement of blood electrolyte contents, pH, urea content and alkaline phosphatase content; slit lamp examination of the cornea; a fat balance test; urine examination with chromatography and simple tests of renal function. From a study of the literature, there appeared to be a strong familial incidence of that condition, with siblings and adults often showing the trait of hypophosphatæmia without skeletal disease; however, many sporadic cases were known, and were explicable on a basis of gene mutation.

Dr. McCoy emphasized that in normal children immobilized for long periods, skeletal decalcification could occur, and that in children with resistant rickets that could lead to hypercalcæmia and its attendant danger of permanent renal damage. It was therefore important to stop vitamin D therapy temporarily during periods of

immobilization following orthopædic procedures. It was also pointed out that deformities should never be corrected till the rickets had been healed, otherwise they would recur. Finally, Dr. McCoy stressed the importance of early diagnosis, and said that vitamin D resistant rickets should always be considered in the differential diagnosis of bowed legs in early childhood. He said that too many of those cases were not recognized till late childhood, by which time little could be done for multiple deformities and retardation of growth.

In summary, Dr. McCoy said that in his paper he had discussed the two current theories of the ætiology of vitamin D resistant rickets, and had presented the typical case of a boy, aged 11 years, whose illness had commenced in the second year of life. Metabolic studies had shown defects in two areas: (*a*) alimentary absorption of bone minerals; (*b*) renal tubular reabsorption of phosphate. He had also stressed the possibility of hypercalcæmia during immobilization, the importance of lifelong maintenance therapy and the desirability of early diagnosis.

DR. H. WILLIAMS said that Dr. McCoy's paper was the result of meticulous investigation involving an immense amount of work. Too many of those patients were referred directly to the orthopædic surgeon. At the present time most cases of rickets were involved metabolic problems, and orthopædic treatment was indicated only when the ætiology had been worked out and the rickets controlled.

DR. H. BREIDAHL said that Dent's theory of the ætiology was an over-simplification; the ultimate answer would probably embrace both theories. It was not understood how those patients tolerated such high doses of vitamin D—doses that would make a normal person very ill.

DR. M. POWELL said that the dosage of vitamin required in those cases varied greatly. He had treated a family in which three siblings had been affected. The first two required dosages of from 150,000 to 200,000 units per day, and both had required osteotomies. The third child, on the other hand, required only 20,000 units per day and had a good figure. Larger doses of from 50,000 to 75,000 units per day had caused toxic symptoms in that child, including thirst, a rash and irritability.

DR. M. ROBINSON asked whether changing the form in which the vitamin D was given was ever advantageous.

Dr. McCoy, in reply, said that Dent had reported that that was so in some cases of post-operative tetany, but there had been no further reports.

Special Correspondence.

PARIS LETTER.

From our Special Correspondent.

WHILST the Academy of Medicine has recently been much preoccupied with the problem of reforming the by-laws relating to medical officers of hospitals in university centres, the Academy of Surgery has calmly been carrying on important discussions on the methods of surgical treatment of stone in the common bile duct. The starting point of this discussion is a communication from Professor Goinard (Algiers),[1] dated November 26, 1958, which described the procedure that he suggested for the surgical treatment of common bile duct lithiasis. Professor Goinard has abandoned all drainage of the main biliary tract; he employs a wedge-shaped resection of the sphincter of Oddi through all its depth by the transduodenal route. When this route is used, in his opinion, the removal of the calculi is easily effected by means of forceps, curettes and scrapers manipulated in the axis of the biliary tract; these instruments can penetrate a long way into the liver. The sphincter of Oddi is cut to a depth of 2 cm.; this section leaves a cavity which makes any external drainage unnecessary. Normally the procedure is preceded by cholecystectomy, and radiomanometry is carried out through the stump of the cystic duct; this permits estimation of the condition of the terminal portion of the bile duct. Professor Goinard considers that only in rare cases is this latter region completely normal. Lesions of the sphincter of Oddi in hepato-choledochal lithiasis are an almost constant finding. They range from œdematous inflammation to sclerotic retractile inflammation of the sphincter. It is only in the rare cases in which radiological examination during operation reveals completely normal permeability of the sphincter of Oddi that the author confines the operation to simple choledocotomy without external drainage. In certain rather uncommon cases there is considerable stenosis affecting several centimetres of the lower end of the common bile duct; in such cases the author recommends a choledoco-duodenostomy. In all other cases—the majority—he recommends the performance of his procedure, which he calls sphincteroplasty.

At the session of March 11, 1959, a debate on the subject began at the Academy of Surgery. The speakers were seven specialist surgeons. The technique described was not particularly severely criticized, but there were a few opinions in favour of greater use of the classical operations and of Kehr's drain. Choledochal reflux following sphincterotomy was held responsible by several speakers for recurrences of cholangitis; but this is by no means a constant observation, and it is far from impossible that post-operative cholangitis attributed to reflux may actually be brought about by wound stenosis. P. Mallet-Guy (Lyon) was the only speaker who opposed the routine performance of Goinard's procedure; in his opinion, operations on the sphincter should be reserved for calculi impacted in the papilla, and the local incision should be limited to what is absolutely necessary for the delivery of the calculus. With this one exception, the majority of the surgeons present appeared to be in favour of operating on the sphincter of Oddi. The only important differences of opinion seem to have concerned the percentage of patients with stone in the common bile duct likely to benefit from this operation.

Convulsive Seizures in the Newborn and in Older Infants of New Ætiology.

Julien-Marie[1] and his co-workers present the case of a neonate who suffered from convulsive seizures of unusual ætiology—convulsions responding to pyridoxin. The seizures occurred in the neonatal period, and the symptomatology presented no unusual features. The behaviour of the child in the interval between crises was unusual; it was characterized by neuro-muscular hyperexcitability and sudden movements of the eyeballs. The outstanding characteristic of these seizures was their constant response to treatment with vitamin B_6. In the case reported, two minutes after the intravenous injection of 10 mg. of vitamin B_6 the child went to sleep; subsequently, large doses of the vitamin were required to prevent the reappearance of convulsive seizures; the daily dosage of pyridoxin necessary to prevent attacks and to maintain normal electrogenesis seems quite characteristic. In the case reported, the maintenance dose was 4 mg. in 24 hours. It was clearly shown that these convulsions are clinically and biologically different from those occurring during states of deficiency of vitamin B_6. The underlying abnormality is a congenital metabolic disorder, in this case affecting the utilization of this vitamin by the central nervous system.

Some New Therapeutic Ideas.

Dehydrating treatment of the dermatoses is recommended by J. Meyer.[2] The author states that water retention is a feature of a number of œdematous affections of the skin, but that it is not always obvious. Infiltration of the mucous membrane, the dermis and the subcutaneous layer may be slight or intermittent, or may occur in the evening only; nevertheless, dehydrating measures, although not the main treatment, do hasten healing. Whether the condition is erythrodermia, artificial œdemato-vesicular dermatitis or infiltrating and pruriginous psoriasis, Meyer suggests treating it with acetazolamide in combination with restricted fluid intake or Kempner's diet. This combination produces dehydration by diuresis in two to four days, and this is the first step in a quick cure. The same technique can be equally well employed in the treatment of dermatitis of the lower limbs associated with varicose veins, and of ulcers of the lower limbs with œdema.

A new antituberculous drug is presented by M. Rist and his co-workers[3]; it is ethylisonicotonic thioamide, or 1314 Th. It is active *in vitro* and *in vivo* against tubercle bacilli resistant to the common antituberculous agents, and especially against those resistant to isoniazid. It is active when given orally. Experimentally, its activity lies between

[1] *Mém. Acad. Chir.* (*Paris*), 1959, 85: 258 (March 11 and 18).

[1] *"La semaine des hôpitaux", Ann. Pédiatrie*, 1959, 35: 1411 (April 24).

[2] *Presse méd.*, 1959, 67: 722 (April 11).

[3] *Presse méd.*, 1959, 67: 625.

that of isoniazid and that of streptomycin. Thus it can replace isoniazid or streptomycin, especially in cases in which the bacilli are resistant to the most generally used antituberculous agents. Laboratory studies prove that resistance to ethionlamide develops as quickly as resistance to isoniazid. The danger of the development of this resistance makes it necessary to give ethionlamide always in combination with another agent which is still active against the patient's organisms. The choice of this second agent is based primarily upon rigorous testing of the sensitivity of the infecting organisms in all cases in which the physician decides to institute treatment with 1314 Th of a patient who has already received other antituberculous drugs. The dose of ethionlamide is approximately 10 to 15 mg. per kilogram of body weight.

A new antidiabetic agent for oral administration, N-N-dimethyl diguanide, is presented by E. Azerad and his co-workers.[1] In one year, more than 100 patients have been treated with it. It is presented in the form of tablets of 0·5 gramme. The initial dosage was 2 to 3 grammes per day, in three or four divided doses. Later the dosage was reduced to the minimum capable of controlling the diabetes (one to three tablets per day). The only disadvantage of the treatment is that it may produce digestive disturbances (nausea, impairment of appetite); but in general these right themselves spontaneously, if the tablets are ingested during meals or if an antacid substance is taken at the same time. In the series there were 22% of failures and 78% of excellent, good or fair results. The best results were obtained with patients aged more than 50 years who were not having insulin; however, good results were also obtained with younger subjects, especially if the diabetes was of recent origin, or if the preceding period of insulin therapy was not too long. These results compare well with those obtained by American workers with a similar substance, phenetyl biguanide.

Secondary failures in the treatment of diabetes with antidiabetic sulphonamides are well known to practitioners. J. Guillon and J. Horeau have made a study of the relative frequency of these secondary failures.[2] When a diabetic, previously well stabilized on oral treatment, experiences an increase in glycosuria and glycæmia after a few months, it is useless to give a much larger dose of antidiabetic sulphonamides. The first step to take is to make certain that the patient has not, consciously or otherwise, been careless with his diet. This is what most commonly occurs, and the reestablishment of strict observance of dietary restrictions, essential to the successful action of the antidiabetic sulphonamides, restores the situation. In that case, the failure of the treatment is apparent, not real. When it is quite certain that a strict diet does not improve matters, then a latent intercurrent infection must be sought as the basis for this secondary resistance to the antidiabetic sulphonamides.

There are, however, rare cases in which treatment with these drugs fails in the absence of any discoverable cause. Often this means that oral treatment has reached its limit. There may be some concern that these failures indicate exhaustion of the pancreas, brought about by the antidiabetic sulphonamides and responsible for an aggravation of the diabetes. This may occasionally happen, but it is highly unlikely if oral treatment is stopped at once when it has been proved ineffective.

The occurrence of these failures is thus no argument against the use of antidiabetic sulphonamides. It simply stresses the need to limit the indications for their use, *to emphasize to the patients the absolute necessity for* observance of dietary restrictions, and to make repeated biological tests in order not to risk prolonging a form *of treatment which appears to have some future risk* attached to it when it is ineffective.

[1] *Presse méd.*, 1959, 67: 765 (April 18).

[2] *Concours méd.*, 1959, 81: 1163 (March 14).

Correspondence.

THE PLAIN FILM SURVEY OF THE ABDOMEN.

SIR: I was interested in the recent article by Dr. Patricia Waugh, and particularly so in the discussion of the source of the fluid which is responsible for the appearance of fluid levels in the plain X rays of patients suffering from suspected intestinal obstruction.

This fluid comes from the digestive juices and that taken orally. These arise above the site of obstruction and bank up behind it, forming little pools in dependent loops of bowel.

Similar little pools will form in various parts of the large intestine following administration of an enema, particularly in children. As an enema is often administered in the ward before a decision to obtain radiographic assistance has been made, it is always a wise thing to inquire about this before giving an opinion on any case of obstruction presenting but few fluid levels upon which the diagnosis may depend.

Yours, etc.

X-Ray Department, The St. George Hospital, Kogarah, N.S.W.
July 2, 1959.
A. D. SMYTHE, M.B., B.S.

THYROID-SUPPRESSIVE DRUGS IN ANGINA OF EFFORT.

SIR: A review of recent literature on cardiac disease shows a marked emphasis on surgery, and neglect of the medical side. For a few years now I have been interested in observing the action of thyroid-suppressive drugs on patients suffering from angina of effort. In all cases I have noted a symptomatic improvement, in some cases amounting to complete freedom from anginal pain, even with marked effort. In fact one patient, although previously recommended to seek the invalid pension as an intractable case, was able to resume work as a bulldozer driver.

The drug of my choice, after trying several, is "Neo-Mercazole", because it has less tendency to enlarge the gland and causes less toxic reactions. I feel that this drug may have an action quite independent of its thyroid-suppressive action, but this is pure surmise. Colleagues who have been discussing this with me have had similar results.

I would be interested to note if others who have been using this drug have drawn similar conclusions.

Yours, etc.

203 Macquarie Street, Sydney.
July 2, 1959.
C. F. LAIDLAW.

REPORT ON A SURVEY OF ALLERGIC REACTIONS TO PENICILLIN.

SIR: May I make a comment on the very excellent "Report on a Survey of Allergic Reactions to Penicillin", as well as a congratulation to the Australian College of General Practitioners on a notable piece of work.

Firstly, the true penicillin allergy, the early delayed reaction. This may persist for a long time, until the last fraction of penicillin is absorbed from the injection site, and may be perpetuated by the penicillin in the milk supply in achlorhydric subjects. Apparently the correct curative treatment now is penicillinase. I was advised in America last year that this was fully effective in four days, but have not yet had a chance to try it personally. It is a rational treatment to destroy the allergen in situ. These people must not have penicillin again.

Second, the serum disease type, the late delayed reaction. It is generally agreed that this is a by-product of the penicillin and is not evidence of penicillin sensitivity, and that it is quite safe for them to have penicillin again. It is my opinion, based on the results of vaccine therapy, that this disorder is due to bacterial allergy, and that a low-grade subclinical sensitivity is brought into hypersensitivity by mass dosage of bacterial products, the result of mass slaughter. Some of these, however, apparently respond to penicillinase.

But most importantly, the shock reaction, possibly anaphylactic—and it is to be noted that anaphylaxis is not confined to allergic subjects. Dr. Feinberg reported at Rio in 1955 that such reactions were increasing alarmingly in frequency, and he told me last year that they were probably three times as common now as then. It is to be noted that this is during a time when the oral antibiotics have been increasingly used in place of penicillin. But it is also to be noted that the first increase occurred

during the time when one dose in 24 hours was adequate, and the second increase has been in the era of "Megacillin" and a three-day interval. It is fairly reasonable to conclude that a considerable proportion of injectees had single-shot treatment in 1953-1955, and that a far greater proportion have had it since. The classical method of inducing anaphylaxis is to inject a foreign protein and then to give a second dose after an interval of 10 days. The classical method of preventing liability is to give the second dose within the 10-day interval.

It seems reasonable to conclude, therefore, that there is a distinct possibility that penicillin anaphylaxis is the result of the single-shot treatment and is preventible by giving a second injection—which need only be a very small one—within the 10-day period. This is standard practice in our clinics now, as it is with ACTH. My attention was first directed to this possibility by the observation that anaphylactoid reactions did occur in patients who had been brought out of the critical phase of allergic diseases by a single mass dose of ACTH, so that the dose was not repeated.

It is, after all, a recognized rule from the antiserum days that this second dose be given within the week, and it seems to me that the rule must be revived and applied to penicillin and other injected antibiotics. It is certainly a "must" with ACTH.

Finally, why is it that most of the patients who claim to get rashes from penicillin say that they are also sensitive to "sulpha" drugs, and is this an illusion? If not, it suggests a further field of work for the College.

Yours, etc.

163 North Terrace, CYRIL T. PIPER.
Adelaide.
June 30, 1959.

SIR: In the "Report on a Survey of Allergic Reactions to Penicillin", published on June 20, 1959, it is stated that: *"The survey officially began on September 1, 1959, and concluded on June 30, 1958."* This is obviously a typographical error, and should be corrected to read: "The survey *officially began on September 1, 1956, and concluded on* June 30, 1958."

Yours, etc.

N. A. ANDERSEN,
Honorary Secretary, Research Committee.
The Australian College of General Practitioners,
New South Wales Faculty,
203 Macquarie Street,
Sydney.
July 13, 1959.

BE IT ENACTED.

SIR: Dr. A. McL. Millar (MED. J. AUST., May 23) is to be congratulated on his careful dissection of medical legislation as it affects each separate State, and his criticism of the lack of coordination by the Commonwealth. Dr. Gavan Gibson (MED. J. AUST., July 4) calls for more freedom and independence and less legislative control.

The Queensland *Medical Act* is held up as a model; but after thirty years of continuous socialist State Government, *medicos have had a surfeit of bureaucratic control—so* much so that recently an attempt by the present Liberal Minister for Health (State) to introduce further controls *was strongly resisted at two general meetings of the* Queensland Branch of the B.M.A., and vehemently so by members who had practised under the English system. *The Minister's attempt was entirely unsuccessful.*

The absence of a Commonwealth register of specialists, combined with Commonwealth intrusion into medical practice *via medical benefits organizations, has led to failure* of uniformity of application of a Commonwealth instrumentality at interstate level. The method of application of *the National Health Act differs in Queensland from the* practice in the other States, an anomaly that definitely conflicts with basic Commonwealth constitutional enact*ments. This has caused unjust hardship to many patients,* particularly those with low earning potential.

There is need for uniformity of medical legislation in *each State, but not involving all the features of the Queens*land Act. It should require little courage by the Commonwealth departments concerned to formulate overriding *legislation to obtain uniformity; but the very slightest hint* of any increase in bureaucratic control or infringement of our liberties should receive unlimited resistance by all practitioners.

"The price of liberty is eternal vigilance." It will take the eternal vigilance of all doctors in this country to withstand the inevitable future endeavours of the opponents of private practice to introduce a socialized national health scheme.

Yours, etc.

149 Wickham Terrace, JOHN A. SHANASY.
Brisbane,
Queensland.
July 10, 1959.

A RELAXING MACHINE.

SIR: In Communist countries with their vested interest in Pavlovian theory, the vogue in treatment of psychiatric disorders is to induce a state of prolonged sleep to provide "protective inhibition". It is claimed that this can be achieved by using a combination of sedative and "tranquillizing" drugs, and the technique has been tried and reported in this Journal (Moore[1]). The title of "sleep therapy" for these drug-induced states has certain seductive implications which many feel are unwarranted.

Other methods of inducing "sleep" have been attempted, and in Communist China a mild electric current is administered for this purpose, through electrodes placed on the head, sometimes over the eyes; once again the experienced are not impressed.

Those psychiatrists who look with disfavour on the excessive administration of electro-convulsive therapy for hysterical patients would welcome some form of treatment *in which their all-too-valuable time is not taken up* listening to people; but no inventive genius has yet been able to devise a satisfactory substitute.

Now a more gentle method of electric treatment has been reported in the last issue of the Journal (Knowles[2]), and this vibrating bed sounds like an apparatus which could help to fill in an otherwise boring hospital day, and provide a fruitful topic for the bridge-table desultory. The bed was given a prolonged trial in a private psychiatric hospital in Brisbane, the patients in the main being hysterics suffering from tension states of varying intensity. The first patient on whom it was used complained of intractable insomnia, and after 30 minutes on the machine slept for two hours. Unfortunately this initial encouraging response was not the usual result, and it was eventually concluded that the bed had no particular advantages over the many reliable and safe drugs which can produce symptomatic relief from nervous tension.

This confirmed Dr. Knowles's impression; but, as he comments in his article, a massive machine with solid *foundations—to produce a wider amplitude of swing and* slower frequency—just may do the trick. The cost would be prohibitive; but perhaps the wealthy crank who *is plagued with insomnia may be interested. A psycho*analysis, however, should be cheaper.

Yours, etc.

Brisbane Clinic, *NEVILLE PARKER.*
79 Wickham Terrace,
Brisbane.
July 6, 1959.

ŒSOPHAGEAL HIATUS HERNIA.

SIR: I am grateful to Mr. C. J. Officer Brown and Mr. Kenneth Morris for their comments on the value of surgery in complicated œsophageal hiatus hernia in the *Journal of May 9, 1959, and congratulate them on their* excellent results, which would not be bettered elsewhere. There is no disagreement on the necessity for operative *intervention when complications warrant it. One still* maintains, however, that careful medical management, not necessarily irksome, gradually reduces the incidence of *complications and necessary surgery.*

In my own experience, stricture complicating œsophagitis is an uncommon cause of dysphagia in adults, and when *it occurs it poses a problem which is equally great to the* surgeon as to the physician. Bleeding from œsophagitis is also uncommon north of the Murray. In 600 consecutive *admissions to Royal Prince Alfred Hospital for hæmate*mesis and melæna over a six-year period, only ten were

[1] *MED. J. AUST., 1957, 1: 9.*
[2] MED. J. AUST., 1959, 2: 15.

found to be bleeding from œsophageal hiatus hernia, and of these only one was gross and that person had an ulcer in the herniated pouch.

There are many fascinating facets about the symptomotology of œsophageal hiatus hernia, not the least of which is the curious periodicity of the œsophagitis. Certainly the last word has not been written on this problem.

Yours, etc.,
S. J. M. GOULSTON.

The Royal Prince Alfred Hospital Medical Centre,
Carillon Avenue,
Newtown, N.S.W.
July 9, 1959.

TONSILLECTOMY.

SIR: Listening this evening to the news broadcast from 2FC at 7 p.m., an official (veterinary) of the University of New South Wales was interviewed on the subject of debarking of dogs. To an inquiry as to the method adopted in this operation, the veterinarian technologist stated that "it was the same as tonsillectomy—the animal was anæsthetized and the vocal cords destroyed by an electric cautery". It would be interesting and instructive to hear from an official (E.N.T.) of the University of New South Wales whether this is accepted practice and the approved method of tonsillectomy laid down for the new medical school.

Yours, etc.,
JOHN S. SMYTHE, M.B., Ch.M. (Sydney).

18 Hay Street,
Collaroy.
June 30, 1959.

THE DRIVER IN RELATION TO THE PHYSIOLOGICAL LIMITATIONS IMPOSED ON HIM AS A HUMAN BEING.

SIR: Dr. Hansman has done good service in calling attention to the limitations of the special senses and to the effects of alcohol in driving. However, I suggest caution about the alerting influences of "constant stream of stimuli" and "a constant variety in the source and intensity of these stimuli", lest these promote mental confusion. Dr. Hansman has made a good point about confusion of stimuli near warning lights and signs. In my experience road signs are generally ample and clear—for those prepared to take heed. Surely the denser the traffic, the slower should be the speed so that one can observe road signs. Before experimenting on the best standards of luminosity of tail lights and reflectors, the authorities might well be more strict about those obviously inadequate in use.

By every reasonable means make the roads safer; but is it not time to pay more attention to the more complex problem of making safer drivers? Good habits can be taught, though I doubt whether more stringent examinations would eliminate foolish and irresponsible conduct on the roads. In my opinion, the problem of safety on the roads turns not so much on the special senses as on common sense.

Yours, etc.
W. S. DAWSON.

B.M.A. House,
135 Macquarie Street,
Sydney.
July 8, 1959.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE ADELAIDE MEDICAL SCHOOL.[1]

[From the *Australasian Medical Gazette*, January, 1896.]

THE Adelaide School of Medicine seems to be in a perilous condition. No sooner have affairs settled down somewhat at the Hospital, where all the mischief that is possible appears to have been done, than clouds appear on the horizon which seem to threaten the well-being of the School and even to imperil its very existence. When the School was first established, only two years out of the five years course were undertaken by the University authorities, but at the instigation of the then Government, and of its Minister of Education, in the following year (1886) a scheme was framed whereby it was possible for the student to complete his course of study at Adelaide. In this scheme reliance was placed on an annual grant of £800 from the Government in lieu of the same amount annually paid for the South Australian Scholarships which were abolished. In 1893 the Government temporarily reduced the amount to £600 but the reduction proved to be permanent. Now it has fallen to the lot of the same Minister of Education, the Hon. J. A. Cockburn, M.D., to announce the withdrawal of this grant. The University has made a solemn and forcible protest against this breach of promise, and we trust that the Government will listen to the appeal, for the University can hardly look, with Iago, upon its purse as trash.

[1] From the original in the Mitchell Library, Sydney.

Notes and News.

Sir Harry Wunderly Appointed WHO Tuberculosis Consultant in Malaya.

Sir Harry Wunderly, former director of the Division of Tuberculosis, Commonwealth Department of Health, Australia, has been appointed Consultant of the World Health Organization (WHO) on Tuberculosis Control for the Federation of Malaya. As WHO consultant, Sir Harry will survey the tuberculosis problem in the Federation of Malaya and advise on the organization of the tuberculosis programme planned for the country.

The University of Adelaide: The Shorney Prize.

The Shorney Prize, established for the purpose of perpetuating the memory of the late Herbert Frank Shorney, M.D., F.R.C.S., Lecturer in Ophthalmology in the University of Adelaide from 1926 to 1933, will be offered for the eleventh time in 1960, and will be for work in diseases of the ear, nose and throat. The relevant clauses of the Statute are as follows:

'3. A post-graduate prize to be called The Shorney Prize, of the value of £100, shall be awarded to the candidate who in the opinion of the examiners has made the most substantial contribution to knowledge in the subjects of ophthalmology or of diseases of the ear, nose and throat.

4. The recipient must be a graduate of an Australian university.

5. The material submitted for the prize may be either a thesis or published work in medical or scientific literature, provided that it shall not have been submitted for examination for a degree, or published, more than five years prior to the closing date of entries for the prize.

6. Each candidate must declare that the work described is his own.

7. The prize shall be offered for competition from time to time as the accumulations of the fund permit.

8. The prize shall be offered at least twelve months before the last day for the receipt of applications.

9. The prize shall not be awarded on any occasion unless in the opinion of the examiners the material submitted is of sufficient merit.

Applications, accompanied by three copies of the evidence which the candidates wish to submit in support thereof, must reach the Registrar, University of Adelaide, not later than July 31, 1960.

Opening of the North Shore Medical Centre.

The North Shore Medical Centre, situated at St. Leonard's, is in certain respects the only one of its kind in Australia. It took shape when the builders, Civil and Civic Contractors, were invited by the General Medical Superintendent of the Royal North Shore Hospital of Sydney, Dr. Wallace Freeborn, to submit ideas on the erection of a modern building near the hospital for use by medical men. Finance for intending buyers has been made available by Lend Lease Corporation, an associate company of Civil and Civic Contractors. Doctors buy their suites on a purchase plan based on a 25% deposit, with the balance payable over a period of 15 years. The articles of association of the Centre are similar to those

of home unit buildings, amended to suit the requirements of the project. The essence of the articles is that holders of a certain group of shares own a specific area in the building.

The Centre was officially opened on June 3, 1959, by His Excellency the Governor of New South Wales, Sir Eric Woodward. In his address, His Excellency said that the Centre would aid decentralization of Sydney's medical facilities; the move to decentralization had begun originally at a centre built near the Royal Prince Alfred Hospital, and the North Shore Medical Centre would carry the move even further. Dr. V. H. Cumberland, representing members of the honorary medical staff of the Royal North Shore Hospital who are associated with the Centre, said that it would place the consultant and the specialist near his major place of work, the teaching hospital. Dr. Cumberland pointed out that such proximity must make for a considerable improvement in the care of the sick, particularly in medical and surgical emergencies. It would also add considerably to the time that consultants would be able to spend in the hospital in the teaching of medical students and resident medical staff. Further, the Centre would act as a landmark for the hospital in its future development, since it was directly opposite the site where is was hoped that the new hospital would be built.

Branches of the specialties represented in the Centre include the following: neurology, psychiatry, pædiatrics, dermatology, allergy, anæsthesia, surgery, neurosurgery, ophthalmology, orthopædics, urology, gynæcology and obstetrics, radiotherapy, radiology and dental surgery The building is seven stories high, with provision for extra floors, and contains 64 suites providing accommodation for doctors. On the ground floor there are a public restaurant, a pharmacy, optical prescription spectacle makers and a travel and estate agency. Each upper floor contains seven standard areas measuring 21 by 16 feet, and two larger rooms each measuring 32 by 16 feet. Many of these sizes have been varied, and the layout within each room is completely flexible. The six upper floors also contain consulting rooms. A special feature is an operating clinic on the first floor. To protect the occupants from the sun, special fibreglass awnings have been installed along the entire length of the buildings, one to each floor. These awnings are an interesting feature in the design as seen from the outside. The ceilings of lobbies, corridors and consulting rooms are sprayed with acoustic "Vermiculite" plaster, which provides both sound and temperature insulation. An unusual feature in the planning of the Centre was the provision of ambulance parking space, so designed as to interrupt as little as possible the flow of traffic on the busy Pacific Highway whilst still permitting access to the Centre of ambulance-borne patients. A substantial awning provides cover for ambulances during wet weather.

A New Child Health Department in Queensland.

The Queensland University and the Queensland Department of Health and Home Affairs are jointly to establish a Child Health Department at the Brisbane Children's Hospital, at a cost of £96,000. Finance for the building will be placed on the Government's 1959-1960 estimates. The department includes a new professorial chair. The professor and his staff are to be new appointees.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

Full-Time Course for Primary F.R.A.C.S.

THE Melbourne Medical Post-Graduate Committee will arrange a six weeks' whole-time course in anatomy, physiology and the principles of pathology for candidates for the Primary F.R.A.C.S., commencing in the middle of January, 1960. This course is designed for candidates who have already studied these subjects extensively by attending organized courses or by private study. It is planned to give the candidates a complete cover of each subject, and to supplement the normal lectures by discussion groups, oral testing and quiz sessions.

Enrolments will be limited to 20 candidates, and will not be accepted on a part-time basis. Applications for the course are to made to the Post-Graduate Committee

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 27, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	3(2)	1(1)	3(1)	..	..	..	..	..	7
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	2	..	1	..	..	..	10	..	13
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1(1)	16(13)	2(1)	..	..	..	1	..	20
Diphtheria	1(1)	..	..	..	1(1)	..	..	..	2
Dysentery (Bacillary)	..	..	1	4(2)	5(4)	..	1	..	11
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	51(20)	25(11)	15(6)	2(1)	..	1	..	..	94
Lead Poisoning	..	..	1	..	..	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	4(1)	..	..	..	..	..	4
Malaria	..	..	1(1)	..	..	..	..	..	1
Meningococcal Infection	2(2)	2(1)	..	..	1(1)	..	..	..	5
Ophthalmia	..	..	..	..	..	..	..	2	2
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	1(1)	..	..	..	..	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	1(1)	1	..	..	2	..	..	5
Puerperal Fever	..	..	..	..	..	..	1	..	1
Rubella	..	14(8)	..	1(1)	2(2)	..	..	..	17
Salmonella Infection	..	..	..	2(2)	..	..	..	..	2
Scarlet Fever	18(4)	19(12)	4(4)	3(3)	3(3)	1(1)	..	..	48
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	21	..	1	..	22
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	30(21)	7(2)	28(13)	3(2)	7(7)	6(3)	..	..	81
Typhoid Fever	..	1(1)	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

not later than October 16, 1959. A fee of £52 10s. will be charged. Forms of application may be obtained from the Post-Graduate Committee at 394 Albert Street, East Melbourne, Victoria.

ROYAL PRINCE ALFRED HOSPITAL: EAR, NOSE AND THROAT DEPARTMENT.

SEMINAR PROGRAMME, 1959.

THE staff of the ear, nose and throat department of the Royal Prince Alfred Hospital will conduct a seminar on the second Saturday of every month at 8 a.m. in the Scot Skirving Lecture Theatre. The main speaker will not exceed forty minutes, and there will be a discussion at the conclusion of his remarks. All medical practitioners and clinical students are invited to attend.

At the next seminar, to be held on August 8, 1959, Dr. V. G. Bulteau will speak on "The Temporal Bone in Head Injuries".

SURGICAL SEMINAR AT ST. VINCENT'S HOSPITAL, SYDNEY.

A SURGICAL SEMINAR will be held at St. Vincent's Hospital, Sydney, on Monday, August 3, 1959, at 5.15 p.m. in the Student's Lecture Hall, fifth floor. The speaker will be Mr. E. G. MacMahon, who will read a paper entitled "Carcinoma of the Breast". The discussion will be opened by Mr. Alan Sharp. All medical practitioners are invited to be present.

Medical Appointments.

Dr. H. E. Pellew has been appointed Honorary Consulting Gynæcologist at the Royal Adelaide Hospital, Adelaide.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Snape, Geoffrey, M.B., B.S., 1957 (Univ. Sydney), 6 Morton Street, Wollstonecraft.

Robinson, Eleanor Mary, M.B., B.S., 1958 (Univ. Sydney), 225 Malabar Road, South Coogee.

Mandula, Esther, M.D., 1925 (Univ. Berlin), M.D., 1927, (Univ. Pecs), 45 Bellevue Road, Bellevue Hill.

The undermentionel have been elected as members of the New South Wales Branch of the British Medical Association (qualifications being M.B., B.S., 1959 (Univ. Sydney) unless otherwise stated): Redwin, Valerie Margaret; McKee, John Douglas; Wilson, Peter Hales; Jones, Charles Finlay; Pain, Michael Cowper Franklyn; Sinnathamby, Sivalingam; Teychenné, John Lever; Bashir, Helen Victoria, M.B., B.S., 1957 (Univ. Sydney); Feller, Keith Hyman, M.B., B.S., 1958 (Univ. Sydney); Langley, Alfred Robert McKenzie, M.B., B.S., 1958 (Univ. Sydney); Willis, Francis Xaxier Morris, M.B., B.S., 1952 (Univ. Melbourne); Wolrige, Lucy Jean, M.B., B.S., 1958 (Univ. Sydney); Upton, John, M.B., Ch.B., 1955 (Univ. Edinburgh).

Deaths.

THE following deaths have been notified:

ANDERSON.—Cauldwell Hamilton Anderson, on July 16, 1959, at Lancefield.

BROWN.—Hedley James Brown, on July 17, 1959, at Brisbane.

DEVINE.—Hugh Devine, on July 18, 1959, at Melbourne.

PHIPPS.—Michael William Phipps, on July 18, 1959, at Mona Vale.

STEVEN.—Arthur Raphael Steven, on July 20, 1959, at Melbourne.

Diary for the Month.

AUGUST 4.—New South Wales Branch, B.M.A.: Organization and Science Committee.
AUGUST 5.—Victorian Branch, B.M.A.: Branch Meeting.
AUGUST 5.—Western Australian Branch, B.M.A.: Branch Council.
AUGUST 6.—South Australian Branch, B.M.A.: Council Meeting.
AUGUST 7.—Queensland Branch, B.M.A.: General Meeting.
AUGUST 11.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
AUGUST 13.—New South Wales Branch, B.M.A.: Public Relations Committee.
AUGUST 14.—Tasmanian Branch, B.M.A.: Branch Council.
AUGUST 14.—Queensland Branch, B.M.A.: Council Meeting.
AUGUST 15.—Victorian Branch, B.M.A.: Country Branch Meeting (Geelong).

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales. Anti-Tuberculosis Association of New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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